Cleft Palate

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

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

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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 cleft palate 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 cleft palate, 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 cleft palate, 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 cleft palate. 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 cleft palate, 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 cleft palate.

The Editors

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

CHAPTER 1. STUDIES ON CLEFT PALATE

Overview

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

The Combined Health Information Database

The Combined Health Information Database summarizes studies across numerous federal agencies. To limit your investigation to research studies and cleft palate, 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 "cleft palate" (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:

- **Cleft Palate Patient: A Challenge for Prosthetic Rehabilitation: Clinical Report**

  Source: Quintessence International. 32(7): 521-524. July-August 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: Although **cleft palate** patients are not regularly seen in general dental practice, their number is not negligible. Prosthodontic treatment of such patients requires good planning that takes into account all remaining teeth and roots, deformation of maxillary segments, residual palatal defects, and the disproportion between the maxillary and mandibular alveolar ridge. With the aim to provide satisfactory function and esthetics and alleviation of the deformities, the authors of this

article describe prosthetic therapy of a **cleft palate** patient using root copings, attachments, telescope and cone crowns, and a metal-base partial prosthesis. The patient's mastication (chewing), phonation (speech), and esthetics (looks) were improved. The authors conclude that successful results can be best achieved through the judicious use of appropriate treatment modalities tempered by clinical experience and creativity. 6 figures. 23 references.

- **Bone Regeneration on the Hard Palate after Palatal Repair on Cleft Palate Patients: A Preliminary Observation**

  Source: Chinese Journal of Dental Research. 5(1): 48-52. 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 observe bony healing on the hard palate after **cleft palate** repair and to discuss the relative factors. Twenty patients with repaired **cleft palates** were examined postoperatively over 5 years. A CT scan of the head was taken in each case. The incidence of bone regeneration among the patients examined was calculated; the position and length of bone tissue were measured according to the CT images. Formation of bone tissue was found in 13 of the 20 patients (65 percent). The sex ratio among the patients was 1 to 1 and there was no obvious difference between cleft types (unilateral or bilateral). The highest incidence of bone formation was in the group of 4 to 6 year olds, and most showed improvement in the premolar and anterior molar areas. The authors conclude that there can be bony healing after palate repair in **cleft palate** patients. 5 figures. 3 tables. 3 references.

Federally Funded Research on Cleft Palate

The U.S. Government supports a variety of research studies relating to cleft palate. 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 cleft palate.

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 cleft palate. The following is typical of the type of information found when searching the CRISP database for cleft palate:

[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: ASPECTS OF BIOTIN NUTRITION**

  Principal Investigator & Institution: Mock, Donald M.; Professor; Biochem and Molecular Biology; University of Arkansas Med Scis Ltl Rock Little Rock, Ar 72205

  Timing: Fiscal Year 2002; Project Start 01-JUL-1985; Project End 31-MAR-2007

  Summary: Long term goals of this project are to determine the biotin requires for normal individuals in circumstances in which biotin status may be impaired and to investigate the consequences and pathogenic mechanisms for marginal biotin deficiency. We recently demonstrated that marginal biotin deficiency is common during normal human gestation and have demonstrated that marginal deficiency is quite teratogenic in mice. Thus, the following five specific aims are relevant and timely. In Specific Aim #1, we will test the hypothesis that maternal biotin deficiency causes abnormal development of fetal skeletons and palate by causing deficient fetal activity of the biotin-dependent enzyme acetyl- CoA carboxylase which leads in turn to deficiency of arachidonic acid and prostaglandin. In fetal palate and limb bud explants from biotin deficient and sufficient CD-1 mice, we will quantitative fetal arachidonic acid component and synthesis rates and will examine the malformation ameliorating effects of supplementation of arachidonic acid and prostaglandin and the amelioration blocking effects of cyclooxygenase inhibitors. Analogous studies will also be conducted in vivo. In Specific Aim #2, we will test the hypothesis that infants with cleft plate or limb shortening have significantly reduced biotin status compared to normal infants. In a case-controlled study, biotin status will be assessed in cord blood using odd-chain fatty acid composition in red blood cell membranes and plasma and lymphocyte activity of the biotin-dependent enzyme propionyl-CoA carboxylase. In Specific Aim #3, we will clone and sequence a biotin transporter recently discovered in our laboratory. In studies of cells from the first individual with biotin transporter deficiency, we will investigate the molecular nature of the genetic defect. In Specific Aim #4, we will confirm promising new indicators of biotin status and investigate the validity of the expression of particular biotin- related genes (e.g., carboxylases) as indicators of marginal biotin deficiency in healthy adults rendered marginally biotin deficiency by egg-white feeding. In Specific Aim #5, we will determine the subcellular localization of the enzyme(s) responsible for catalyzing the beta- oxidation of biotin to the inactive metabolite bisnorbiotin and characterize this pathway. Understanding of this pathway is important because accelerated biotin catabolism may be the major cause of biotin deficiency in pregnancy and anticonvulsants.

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

- **Project Title: BIOBEHAVIORAL NEUROSCIENCES IN COMMUNICATION DISORDERS**

  Principal Investigator & Institution: Rice, Mabel L.; The Fred and Virginia Merrill; Bureau of Child Research; University of Kansas Lawrence Youngberg Hall Lawrence, Ks 660457563

  Timing: Fiscal Year 2002; Project Start 23-SEP-2002; Project End 31-AUG-2007

  Summary: (provided by applicant): The BNCD Center is comprised of 15 affiliated research projects, with 12 individual investigators, 10 of whom are funded by NIDCD, 2 from NICHD, 2 from NIA, and 1 from NIDCR, with a current year funding level of $3,019,989. The individual research projects involve studies of symptoms, etiology, diagnosis of and intervention with language impairments in children, sensor motor aspects of speech production in infants and children, speech and lexical representations in children and adults, age-related communicative decline in elderly adults, infant

visual neuroperceptual development as a predictor of later cognitive development, and cochlear functioning of the auditory system. Disease entities include speech and language impairments and associated reading difficulties of children and adults; mental retardation; autism; **cleft palate;** sensor motor impairments to infant or facial mechanisms; hearing loss; aging; and dementia. Outcomes of the investigators' research programs include an identified clinical grammatical marker of SLI with a newly published standardized assessment instrument for clinical uses; a device for measuring infant's or or facial sensor motor functioning; an identified infant attention marker as a predictor of developmental cognitive risk; an identified clinical linguistic marker of dementia/Alzheimer disease; a model of cochlear pathology with direct links to hearing aid design; and a model of possible cochlear neuroregenerative processes with implications for biointervention in hearing disease. The Center provides support for current and future research, and new collaborative research, via an Administrative Core with specialized information retrieval and dissemination services, and three research cores: Advanced Statistical Methods (ASC), Participant Services (PARC), and Digital and Electrical Engineering (DEEC).

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

- **Project Title: BIRTH DEFECTS TREATMENT AND PREVENTION PROGRAM**

  Principal Investigator & Institution: Murray, Jeffrey C.; Professor; Pediatrics; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 17-AUG-2001; Project End 30-APR-2006

  Summary: (Provided by applicant): Cleft lip and **cleft palate** can serve as a sentinel for birth defects in general for the impact that they have on fetal and maternal health. As sentinels, they are easy to identify and require a high input of surgical and medical care, but also commonly result in long-term survival of affected individuals, even when untreated. They are common with the average frequency of about 1:1000 in most South American countries. Their etiology is complex, although it is clear that genes and genetic and environment interactions play an important role. Nutritional factors in clefts are well recognized and have been studied for over 40 years. Recent evidence that folate or B6 deficiency, as well as a role for smoking and alcohol use, suggest that environmental interventions in the form of supplementation or preventive strategies may be effective in decreasing the frequency of these birth defects. The South American birth defects registry, Estudio Collaborativo Latinoamericano de Malformaciones Congenitas (ECLAMC), has for many years provided epidemiologic information on the frequency of birth defects throughout South America. At the present time, folate supplementation has been introduced to one country in South America (Chile) and it is now possible to measure changes in outcomes of this based around the known preventive effect of folic acid supplementation for neural tube defects and the likely effect that it may have on cleft lip and **cleft palate.** Extensive populations of affected individuals such as those followed by the Centrinho clinic in Bauru provide high risk populations in which targeted interventions can be effectively studied. In this proposal, the applicants will use cleft lip and **cleft palate** as a sentinel defect to study the impact of birth defects in general on maternal, fetal and neonatal health and to carry out direct interventions on decreasing the number of these birth defects using both behavioral and medical interventions. The specific aims will include measuring the impact of the interventional use of folic acid supplementation on cleft lip and **cleft palate** and neural tube defects, measuring the impact of having a child born with a cleft on subsequent maternal, infant and family health, and finally, interventions to decrease the number of birth defects through the direct prevention strategies of smoking intervention and vitamin

supplementation. The outcome of this project will be to further strengthen collaborative relationships in the area of craniofacial anomalies between Brazil and the US, to better understand the effects of birth defects and craniofacial anomalies in particular on maternal family units and to decrease the burden of these defects directly.

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

- **Project Title: BRAIN STRUCTURE/FUNCTION IN OROFACIAL CLEFTING DISORDERS**

  Principal Investigator & Institution: Nopoulos, Peggy C.; Professor; Psychiatry; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 01-APR-1999; Project End 30-MAR-2004

  Summary: Clefts of the lip and palate are developmental craniofacial abnormalities that result from a failure of neural crest cells to migrate properly. As a group, clefting disorders are comprised of those that are isolated to facial clefts only (non-syndromic) and those in which the facial cleft is part of a well-defined syndrome of additional anomalies. Non-syndromic clefting has been shown to be associated with cognitive dysfunction. In syndromic clefting disorders, cognitive dysfunction is ubiquitous and often severe. The fact that clefts of the lip and/or palate are associated with brain abnormalities is intuitive as the development of the brain and face are intimately related. However, the systematic study of the types of brain anomalies present in patients with clefts of the lip and/or palate (and the functional consequences thereof) has been almost completely overlooked. This is an application for a Mentored Patient Oriented Research Career Development Award. During the award period, the candidate proposes an organized program of training and supervised research. While the candidate has training in structural imaging of the brain, she requires additional training in developmental biology, cognitive assessment, clinical assessment of genetic syndromes, and molecular and quantitative genetics. This training will be integrated with a research project in which the candidate proposes to phenotype Van der Woude Syndrome (VDWS), an autosomal dominant disorder manifesting as isolated clefts of the lip and/or palate and lip pits, by: 1) evaluating brain structure of patients using Magnetic Resonance Imaging, and 2) evaluating brain function in these patients using neuropsychological tests. In addition, these patients with VDWS will be screened for microdeletions using an allele loss assay. This will allow direct phenotype/genotype correlations to explore the relationship between the genetic determinants of facial clefting and brain structure/function. These findings will lead to a better understanding of the neurobiology underlying the cognitive dysfunction that significantly impairs the life of many patients with facial clefts. In turn, these findings may lead to early intervention with detection and treatment of cognitive deficits. This award would provide the candidate with the necessary background for further studies into brain structure and function in other craniofacial syndromes as well as into the genetic determinants of brain development. This award will also provide the candidate with the background necessary for ongoing research and funding leading to an independent research career.

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

- **Project Title: CHARACTERIZATION OF THE MOUSE CPO1 MUTATION**

  Principal Investigator & Institution: Bjork, Bryan C.; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

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

Summary: (provided by applicant): Non-syndromic cleft secondary palate (CP) is one of the most common human birth defects. It has a very complete etiology that includes strong genetic, likely polygenic, and environmental contributions. Although many embryological studies in model organisms and linkage and association studies in humans have provided insight into this complexity the developmental and genetic basis for normal palate development remains incompletely understood. The study of palatal development in isogenic mouse strains carrying Mendelian mutations in a controlled environment avoids confounding influences as allelic heterogeneity and environmental insults. Specifically, I propose to initiate studies of mouse mutation with an isolated cleft secondary palate phenotype, **cleft palate** only 1 (cpo1), as an entry point into the understanding of a specific gene whose function and interactions in a genetic pathway(s) is essential to norm; palatogenesis. I have used a positional cloning strategy to rapidly clone the causative gene for cpo1, the Prdm16 (alias, Mel1) Zn-finger transcription factor. I will use the cpo1 mutant to elucidate the specific developmental defect in palatogenesis caused by the Prdm16 gene mutation and analyze the pattern of Prdm16 gene and protein expression during embryogenesis and palatogenesis in wildtype mouse embryos. Using in situ hybridization and immunohistochemistry, I will assay the expression of genes and proteins that mark specific stages and structures during palatogenesis to identify putative members of a common genetic pathway affecting normal palate development. Finally, downstream targets and DNA-binding sites of the Prdm16 protein will be identified through hybridization to DNA binding arrays and co-immunoprecipitation experiments.

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

- **Project Title: CHILDREN WITH CLEFT LIP AND PALATE**

  Principal Investigator & Institution: Richman, Lynn C.; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002

  Summary: This study is designed to examine the relationships of risk factors for children with non-syndromic cleft lip and palate (CL&P) to psychological adjustment. The objective is to determine which risk factors have a primary influence on the behavioral inhibition or shyness seen in many children with CL&P. The specific aims are to determine how facial appearance and speech contribute to behavioral adjustment and how other individual characteristics such as verbal expression deficit and auditory memory deficits may affect the relationship. Also, it is planned to perform a behavioral analysis and intervention to determine if excessive behavioral inhibition occurs in all situations and whether it is modifiable. The analyses will compare children with CL&P, who have different forms of behavioral inhibition and determine if differences are related to the risk factors. Predictive equations will determine how much early characteristics of verbal disability or memory deficit versus speech and facial appearance contributes to behavior inhibition and possible anxiety.

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

- **Project Title: CLONING AND CHARACTERIZATION OF THE VAN DER WOUDE GENE**

  Principal Investigator & Institution: Schutte, Brian C.; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 10-JUL-2002; Project End 31-JUL-2002

Summary: Cleft lip and palate (CL/P) is a major congenital structural anomaly that is notable for significant lifelong morbidity and complex etiology. The extensive psychological, surgical, speech and dental involvement emphasize the importance of understanding the underlying causes. For the investigator, cleft lip and palate, like other complex diseases, provides a challenge in determining the multiple genetic, environmental and stochastic factors that lead to its phenotype. In this proposal, we will pursue the complex causes of cleft lip and palate through our investigations of a genetically simple form of clefting, Van der Woude syndrome (VDWS). VDWS is the most frequent syndromic form of cleft lip and palate and the form we fell is best suited to contribute to an increased understanding of the more common non-syndromic form of cleft lip and palate and the form we feel is best suited to contribute to an increased understanding of the more common non-syndromic form. Specific goals in this project will include: 1) identification of the VDWS gene. A genetic screen for disease-causing micro-deletions will be used to further restrict the region that contains the VDWS gene. Powerful gene-finding techniques, including the sequence analysis of the entire critical region, will be used to identify transcriptional units. Mutation screens will then be used to find disease causing changes in the DNA. Extensive mutation screens will be performed to search for functional domains. 2) characterization of the VDWS gene and its mouse homolog, including complete cDNA and genomic sequence analysis, the study of temporal and tissue-specific expression to identify developmental pathways that require the VDWS gene functional and screens for gene homologs which may function in the same pathway. 3) identification of sequences that regulate VDWS gene expression and the development of transgenic mouse models, including a mouse knockout that will be used in 4) long-term studies that will include complementation experiments to identify other genes in the pathway and investigate the effects of environmental factors on the VDWS gene and other genes in the same pathway. The impact of this project is that studies of CL/P are valuable, both for the importance of the defect itself as a contributor to morbidity and for providing a model for a complex human birth defect. The identification of the VDWS and VDWS-like genes will immediately provide for better risk counseling, and their characterization under environmental stresses hold the promise for contribution to preventative strategies and improved therapeutics. In addition, the identification of the VDWS gene is relevant to studies of CL/P because of its similarities to the more frequent non-syndromic forms of CL/P and because it will provide a foothold into the earliest steps of craniofacial development.

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

- **Project Title: CONTEXT FOR FILIPINO CB CLEFT PREVENTION INTERVENTIONS**

  Principal Investigator & Institution: Daack-Hirsch, Sandra; None; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2003; Project Start 01-JAN-2004; Project End 31-DEC-2006

  Summary: (provided by applicant): The purpose of this proposal is to obtain contextual data prior to planning for community-based (CB) interventions in the Philippines aimed at informing people about causes and preventing orofacial clefting. In the Philippines, 1/500 live born children will have a cleft lip with or without a **cleft palate.** Here there is a high prevalence of clefting and treatment is limited or unavailable. Anthropological reports describe Asian beliefs about the cause of illness as supernatural. If Filipinos hold this belief then interventions inconsistent with their understanding of cause and prevention may not be accepted. Therefore, an ethnographic study is warranted to

describe attitudes and beliefs regarding the cause, prevention and treatment of clefting. Using an explanatory models framework, qualitative methods will be used to describe current beliefs about the causes, prevention and treatment of orofacial clefting, and willingness to participate in prevention trials of orofacial clefts among Filipinos and health care workers. In-depth interviews will be conducted with people who have a cleft or child with cleft, people who neither have cleft or children with cleft, and Filipino health workers. Interviews will be coded for broad categories. More specific descriptive sub-codes will be assigned to the data grouped under the broad categories. Data will be analyzed for regularities in terms of themes or concepts within each group and across the three groups.

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

- **Project Title: COPING WITH CRANIOFACIAL DISORDERS**

  Principal Investigator & Institution: Slifer, Keith J.; Kennedy Krieger Institute, Inc. 707 N Broadway Baltimore, Md 21205

  Timing: Fiscal Year 2002

  Summary: Children with craniofacial disorders have increased incidence of anxiety, withdrawal and social competence problems, but they tend to rate their own appearance more positivity than it is rated by others. Some may learn to cope with facial impairment by minimizing it an developing compensatory behavior. Direct observations of these children reveal social interactions that differ significantly from peers. Other data suggest they have impaired ability to communicate emotion through facial expressions. This study will employ: (1) microanalytic direct observation methods, and (2) computer-automated recognition of facial expressions to quantify the social and facial behavior of 8 to 16 year-old subjects videotaped during: (1) an analogue social interaction with a confederate peer, and (2) a structured facial encoding task. Results will be compared across matched Craniofacial (oral cleft and craniosynostosis). Non-facial (short stature), and Normal Control groups. Within-group comparisons will examine ow subjects with positive self-perceptions differ from those with comparable physical impairments and average or negative self-perceptions. Differences in self ratings of appearance and self-concept are expected to be significantly correlated with observable differences in social behavior. Craniofacial subjects (particularly those with oral clefts) are expected to evidence impaired ability to encode emotion through facial expressions. Some differences in social and facial behavior may reflect compensatory behavior developed by those who are better-adjusted and more socially competent, which could be taught those who are less competent. If differences in ability to generate facial expression are found in subjects with craniofacial disorders, and associated with impaired social competence, the results may lead to assessment techniques for detecting subtle but clinically significant facial dysfunction. Some may be amenable to surgical correction, others to behavioral intervention (e.g. response shaping with reinforcement contingencies or biofeedback training of facial muscles). Such intervention could be tested by subsequent demonstration projects. The combined results will provide an empirical basis for selecting specific skills to be taught in future prospective interventions for children with craniofacial disorders.

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

- **Project Title: DENTAL AND ORTHODONTIC ACCESS IN CRANIOFACIAL CARE**

  Principal Investigator & Institution: Cunningham, Michael L.; Director; Children's Hospital and Reg Medical Ctr Box 5371, 4800 Sand Point Way Ne, Ms 6D-1 Seattle, Wa 98105

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

Summary: (provided by applicant): The ability of children with special health care needs to access dental care is an understudied area. Access to dental and orthodontic care for children with craniofacial disorders is of particular importance since these children require dental and orthodontic care as a direct result of their medical condition and as an essential part of their reconstructive treatment. The overall objectives of this study are to develop tools to characterize barriers to accessing dental and orthodontic care for patients with craniofacial disorders and to identify potential strategies by which access to care may be improved. With that in mind, four specific aims are proposed. In the first project, instruments will be developed, using information obtained from key informant interviews of patients and families, to identify and characterize barriers to accessing timely and appropriate dental and orthodontic care for children with craniofacial disorders. In the second project, Washington state Medicaid claims data will be analyzed to characterize dental and orthodontic care utilization and travel distance for care for low-income children with cleft lip and/or palate. Areas of Washington State where Medicaid beneficiaries with craniofacial disorders have difficulty accessing local dental/orthodontic care will be identified. In the third project, a statewide survey will be developed to assess current level of involvement of community orthodontists in caring for children with craniofacial disorders and to identify factors that could potentially promote or impede increased participation in the future. In the final project, models of patient advocacy programs will be identified and collaborations between the Law School and the Craniofacial Center will be developed with the goal of developing an advocacy program aimed at improving access to dental and orthodontic care for children with craniofacial disorders. At the completion of this planning grant period, we will be prepared to implement a large scale assessment to characterize barriers to accessing dental and orthodontic care and their consequences, as well as intervention projects specifically targeted at the barriers we identify. The overarching goal of the subsequent full-scale project will be to improve access to dental and orthodontic care and thus promote optimal outcomes for all children with craniofacial disorders. This model could potentially be applied to children in other states and to other groups of children with special health care needs.

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

- **Project Title: DEVELOPMENT OF THE PALATE AND CRANIOFACIAL MESENCHYME**

  Principal Investigator & Institution: Hay, Elizabeth D.; Professor; Cell Biology; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-AUG-1994; Project End 31-JUL-2004

  Summary: (adapted from the Investigator's abstract): The broad objective of this application is to understand the tissue transitions involved in the development of the palate and craniofacial mesenchyme. Transformation of the medial edge epithelia (MEE) to mesenchyme in the paired palatal shelves from avian and rodent models will be examined. This represents a model for embryonic tissue remodeling and has potential importance to better understand failure of the palatal shelves to fuse in humans. The Principal Investigator's laboratory was the first to propose and demonstrate that the MEE undergoes epithelial-mesenchymal transformation (EMT) after fusing to form a midline seam, and that the resulting mesenchymal cells become part of the palate connective tissue, thus establishing confluence of the palatal stroma. It is likely that EMT is involved in other craniofacial processes where epithelial fuse, consequently studies are proposed to examine the formation of the upper lip. Understanding the cellular

mechanism of palatal EMT will result in new approaches to defining the causes of congenital facial anomalies, such as **cleft palate** and other facial clefts that may result from failure of the EMT process. The specific aims are to study (1) the role of cell-cell contacts between opposing palatal shelves in initiation of EMT in the MEE; (2) the role of cell-matrix interactions and TGF-beta3 in the emigration phase of EMT; and (3) the role of defective EMT in **cleft palate** and in cleft lip. It is expected that beta-catenin and plakoglobin associated with the newly formed MEE junctions are the signaling molecules involved in initiating palatal EMT. Also it is expected that matrix-stimulated tyrosine kinases interact with growth factors at the plasmalemma level to promote emigration. Knowledge of the basic cell biology will lead to more effective treatment of human facial clefting.

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

- **Project Title: DGAP: DEVELOPMENTAL GENOME ANATOMY PROJECT**

  Principal Investigator & Institution: Morton, Cynthia C.; Professor; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-APR-2001; Project End 31-MAR-2006

  Summary: (Applicant's Abstract): The goal of the Developmental Genome Anatomy Project (DGAP) is to identify genes critical in human development that are disrupted or dysregulated by balanced chromosomal rearrangements in humans with multiple congenital anomalies. Approximately 1 in 2000 newborns has an apparently balanced rearrangement, with a 6.1 percent risk for a serious congenital anomaly. These anomalies can include isolated defects ranging from cleft palate/lip, abdominal wall defects, limb defects, cardiac abnormalities or mental retardation, or they can occur as part of clinically recognizable syndromes. Of particular relevance is the fact that de novo structural abnormalities involving all chromosomes have been reported in association with congenital anomalies; it has been speculated that a significant number of such chromosomal breaks directly disrupt or dysregulate genes critical to specific molecular pathways. We propose to study individuals with multiple congenital anomalies and apparently balanced chromosomal rearrangements, with the aim of using balanced chromosomal rearrangements as signposts to identify these critical genes. The potential of DGAP will be greatly enhanced by rapidly evolving genomic resources including the complete human DNA sequence and an ordered FISH BAC map of the human genome. Collaborations established between cytogeneticists and clinical geneticists across the medical genetics community have been established to collect patient samples with a variety of developmental defects and balanced chromosomal rearrangements. Analysis of chromosomal breakpoints through FISH mapping studies will be used to identify single genomic clones containing relevant candidate sequences, and an online DGAP database is being created (Project 1). Molecular identification and analysis of candidate genes, as well as mutation studies in affected individuals will be the focus of subsequent studies (Project 2). Identification of expression patterns assessing tissue or temporal specificity will follow, as well as isolation of homologs in M. musculus and D. melanogaster (Project 3). Ultimately, transgenic animals will be used to study specific clones of interest to elucidate more fully their role in development (Project 3). DGAP constitutes a multi-laboratory and multi-institutional research endeavor which brings together the disciplines of clinical genetics, cytogenetics, molecular biology and developmental genetics to illuminate genes involved in fundamental pathways during human development.

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

- **Project Title: DISSECTION OF THE VCFS PHENOTYPE--PALATAL ANOMALIES**

  Principal Investigator & Institution: Mitchell, Laura E.; Professor; Children's Hospital of Philadelphia 34Th St and Civic Ctr Blvd Philadelphia, Pa 19104

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

  Summary: Velocardiofacial syndrome (VCFS) is a multiple malformation syndrome that is associated with a deletion of chromosome 22q11 in the majority of patients. The VCFS phenotype includes a broad range of features, but is most commonly characterized by the tetrad of palatal anomalies, congenital heart defects, cognitive impairment and a typical facial appearance. Individuals with VCFS usually exhibit only a subsets of these features, and the specific nature of any given feature may differ between individuals. For example, palatal anomalies are observed in approximately 50% of patients with VCFS and include overt **cleft palate,** submucous **cleft palate,** bifid uvula and velopharyngeal dysfunction. It was originally hypothesized that differences in the size of the chromosome 22q11 deletion would explain the observed variability in the VCFS phenotype. However, deletion size has not proven to be a strong phenotypic predictor, indicating that other factors-such as individual differences in genetic background and/or exposure history-must contribute to the observed variability in the VCFS phenotyped. Studies to identify specific factors that influence the VCFS phenotype will require extensive, systematically collected data from several hundred patients. We are uniquely poised to conduct studies of this nature, since the requisite data will be available through the proposed program project. The proposed project will capitalize on these data to identify the factors that influence the palatal phenotype in patients with VCFS. A comprehensive approach, integrating molecular and clinical data from patients with VCFS, will be employed to identify these factors. The proposed analyses will greatly increase our understanding of the factors that influence the palatal phenotype in patients with VCFS, and will lay the foundation for similar analyses of other phenotypic features of this syndrome.

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

- **Project Title: ECM, INTEGRINS, AND ACTION IN SALIVARY MORPHOGENESIS**

  Principal Investigator & Institution: Larsen, Melinda; U.S. Nat'l Inst/Dental/Craniofacial Res Dental & Craniofacial Research Bethesda, Md 20892

  Timing: Fiscal Year 2002; Project Start 01-SEP-2002

  Summary: (provided by applicant) Branching morphogenesis is a complex process that occurs during the development of the salivary gland, lung, kidney, prostate, and mammary gland. Using the salivary gland organ culture system, some molecules required for branching have been identified, including integrins, the extracellular matrix (ECM), and the actin cytoskeleton, but mechanisms remain unclear. The first step in branching is formation of clefts in the epithelial surface. Collagen III has been localized to clefts, indicating it may play a role in cleft formation. Integrins are heterodimeric molecules, which span the plasma membrane and mediate interaction of the ECM with the actin cytoskeleton and are, therefore, likely involved in coordinating cell movements and/or shape changes involved in branching morphogenesis. This proposal will address the role of integrins and actin cytoskeleton in submandibular gland development with three specific aims: 1) identify the role of collagen III in cleft formation, 2) define the actin rearrangements and regulators required for cleft formation, and 3) determine if there is an adhesion complex assembled at the sites of cleft formation. Understanding the composition and function of cell-matrix contacts in salivary branching morphogenesis will lead to further understanding of complex developmental processes

and provide insights that may facilitate development of rational approaches for salivary gland regeneration in cancer and Sjogren?s syndrome patients.

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

- **Project Title: EPITHELIAL/MESENCHYMAL TRANSFORMATION IN PALATOGENESIS**

  Principal Investigator & Institution: Shuler, Charles F.; Professor and Director; University of Southern California 2250 Alcazar Street, Csc-219 Los Angeles, Ca 90033

  Timing: Fiscal Year 2002

  Summary: A critical event in the fusion of the secondary palate is the disappearance of the medial edge epithelium from the midline. Studies in our laboratory have used cell lineage analysis to trace the fate of the medial edge epithelial cells and document that these cells undergo a phenotypic transitions and remain viable as mesenchymal cells. Investigations of the molecular control of the phenotypic transformation have identified TF-beta3 as an important regulating molecule. Homozygous TGF-beta3 knock-out mice do not fuse in organ culture without supplementation of exogenouse TGF-beta3. These findings have led to the hypothesis, TGF-beta3 is a primary effectors molecule responsible for initiating the program of epithelial-mesenchymal transformation in the palatal shelf medial edge epithelial cells during palatal fusion. This hypothesis will be tested by four Specific Aims; 1. To determine the role of TGF-beta3 in the pattern of expression of cell-type specific phenotypic markers in the MEE during palatogenesis; 2. To characterize the mechanism of TGF-beta3 regulation of the cell cycle and MEE cell proliferation prior to palatal shelf contact and the onset of epithelial-mesenchymal transformations; 3. To examine the intracellular signalling pathway in the MEE following binding of the growth factor to its cell surface receptor; 4. To evaluate TGF-beta3 regulation of matrix metalloproteinases in the mesenchyme underlying the MEE responsible for degradation of the basement membrane. Identification of molecular mechanisms essential to the process of palatal fusion will result in future possible applications to determining the mechanisms underlying human craniofacial birth defects, developing prenatal diagnosis strategies, establishing familial risk of craniofacial birth defects, determining the mechanism of action of craniofacial teratogens and reducing the incidence of human craniofacial birth defects.

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

- **Project Title: EUSTACHIAN TUBE FORM/FUNCTION IN CLEFT LIP AND PALATE**

  Principal Investigator & Institution: Gungor, Anil; Children's Hosp Pittsburgh/Upmc Hlth Sys of Upmc Health Systems Pittsburgh, Pa 15213

  Timing: Fiscal Year 2003; Project Start 01-MAY-2003; Project End 30-APR-2005

  Summary: (provided by applicant): Non-syndromic clefts of the lip and/or palate are among the most common malformations of the head and neck. Hearing loss and otitis media and effusion (OME) are common in **cleft palate** (CP patients because of poor Eustachian tube (ET) function resulting from hypoplasia and malpositioning of the palatal muscles, hypoelasticity of the ET cartilage and neuromuscular immaturity. One goal of palatal reconstruction is to establish more normal muscle vectors and attachments so as to improve tubal function and prevent future OME episodes. Unfortunately, that goal has not been realized because of a limited knowledge of the anatomical foundation for ET function. Recent methodological advances for evaluating ET function and for in vivo assessment of soft tissue anatomy hold much promise to address that deficiency. In the proposed study, quantitative magnetic resonance

imaging (MRI) measurements of the ET and paratubal muscles in combination with measurement of ET function will be used to develop the form-function identity for the ET system in CP patients. Specifically, we will enroll 40 children aged 7-10 years with repaired, unilateral and bilateral complete CP (n+20/group) and with and without tympanostomy tubes for persistent OME (n=10/subgroup). Each child will have an MRI to define ET anatomy and a comprehensive battery of ET function tests to assess function. These data will be compared to those available for non-CP patients and analyzed for consistency with predictions that: 1) compared to age matched non-CP patients. CP patients have a hyperplastic ET cartilage, undeveloped paratubal muscles, aberrant origins and/or insertion for those muscles, greater ET compliance and poorer muscle-assisted ET opening: 2) the relative degrees of poor function and abnormal morphology are graded with the unilateral complete CP patients having lesser deficiencies than the bilateral complete CP patients: 3) the degree of functional impairment in these patients is directly related to the degree of anatomical deficiency, and 4) the anatomical deficiencies noted for CP patients with patent tympanostomy tubes are more extreme than those in the age-matched CP patients without a tympanostomy tube and no recent history of OME. If these predictions are valid, an early MRI study of CP infants be prognostic of the severity and longevity of ME disease and may serve to guide the type of palatal reconstruction for individual patients.

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

- **Project Title: FOLATE PATHWAY GENES AND RISK FOR OROFACIAL CLEFTS**

  Principal Investigator & Institution: Shaw, Gary M.; Research Director; March of Dimes Birth Defects Foundation 1900 Powell St, Ste 1050 Emeryville, Ca 946081836

  Timing: Fiscal Year 2002; Project Start 01-SEP-2000; Project End 30-APR-2004

  Summary: The research program will investigate nutritional and genetic risk factors for orofacial clefts. The specific aims for the 3-year study are to assess the potential "gene-environmental" interplay between genetic variation of 3 potential folate pathway genes (folate receptor gene, reduced folate carrier, and the N-acetal transferace 1 gene) among probands, maternal folic acid/multivitamin intake, and the risk of orofacial clefts. We propose to investigate the hypothesis that one or more of the 3 folate pathway genes are responsible for inadequate transport, accumulation, or metabolism of folate during critical stages of craniofacial development, making embryos susceptible to orofacial clefts even in the presence of clinically adequate maternal folate intake. By combining state-of-the-art molecular biology approaches, new genetic findings, and one of the largest case-control studies done on orofacial clefts, we will determine if maternal supplemental folic acid intake overcomes folate transport or metabolic dysfunction that may occur as a result of the embryo's genotypic variation for the 3 folate pathway genes and thus reduce the risk for orofacial clefting. The project has 3 collaborating research centers: California Birth Defects Monitoring Program, University of Nebraska, and Children's Hospital, Oakland. The research design will be case-control, including approximately 1200 cafes and controls, and will utilize maternal interview data in conjunction with genotyping of the folate receptor gene. Infants' DNA for genotyping will be obtained from residual newborn screening bloodspots, of which about 1250 DNA samples will be available for this study. Information on a variety of relevant covariates, such as parental cigarette smoking and the infant's genotype for transforming growth factor-alpha polymorphisms, will be available to analytically assess their contribution to risk for orofacial clefts. As one of the first attempts at investigating environmental and molecular genetic interactions in the epidemiology of congenital anomalies, this study endeavors to enhance our general understanding of the

causes of orofacial clefts as well as our specific understanding of the apparent protective effect of folate supplementation on the occurrence of clefts. We observed a 50% reduction in risk for orofacial clefts among pregnant women who used vitamins. If this association ultimately proves causal, many of these anomalies will be preventable every year in the United States once it is understood what vitamin/diet component is important in facilitating the reduction in risk.

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- **Project Title: FOXC2 IN HEREDITARY LYMPHEDEMA AND LYMPHATIC DEVELOPMENT**

  Principal Investigator & Institution: Glover, Thomas W.; Professor; Human Genetics; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2002; Project Start 01-JUL-2002; Project End 30-APR-2006

  Summary: (provided by applicant): The hereditary lymphedemas are developmental disorders of the lymphatic system that lead to disfiguring and often disabling edema (swelling) of the extremities together with various associated abnormalities. Most are autosomal dominant with variable expression and age of onset. The primary target tissue in these conditions is the lymphatic system, a poorly understood component of the vascular system responsible for microcirculation of fluids drained from tissues and the return to the blood vascular system, and for trafficking cells of the immune system. Despite its importance in congenital and acquired disease, including cancer, very little is known about the molecular events involved in development of the lymphatic system. As with many other developmental pathways, genes involved in hereditary lymphedema can provide important insights into the molecular events Involved in lymphangiogenesis. We recently identified the gene responsible for hereditary lymphedema-distichiasis (LD). This disorder is characterized by lymphedema and extra rows of eyelashes arising from the Meibomian glands. Associated abnormalities include tetralogy of Fallot, **cleft palate,** hydrops fetalis and cystic hygroma. The gene responsible for LD is the FOXC2 forkhead family transcription factor. The overall goals of this project are to determine the role of FOXC2 in hereditary lymphedema and in the development of the mammalian lymphatic system. Preliminary data indicates that Foxc2+/- mice have highly abnormal lymphatic vessels and lymph nodes analogous to those in patient's with LD. Specific aims are: (1) to fully characterize Foxc2 +/- and -/- mice, and transgenic mice overexpressing the gene, for lymphatic abnormalities as a model system for lymphedema-distichiasis and abnormal lymphatic development in mammals; (2) to determine the expression patterns of Foxc2 in the lymphatic system during development to begin to assess the mechanism of Foxc2 insufficiency on lymphatic phenotype and development; (3) to begin to establish the role of Foxc2 in the pathways and hierarchy of genes controlling lymphangiogenesis in mammals; (4) to assess the timing of Foxc2 deficiency in lymphatic and other abnormalities by creating mice in which Foxc2 is conditionally expressed during development. From these studies we will learn the precise defects in the developing mouse lymphatic system caused by Foxc2 deficiency, whether Foxc2 expression in lymphatic or other cell types is correlated with these defects, the timing of Foxc2 insufficiency on phenotype, and will begin to determine the role of Foxc2 in the complex biochemical pathways involved in lymphangiogenesis.

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- **Project Title: FUNCTIONAL ANALYSIS OF ACTIVINS DURING DEVELOPMENT**

  Principal Investigator & Institution: Matzuk, Martin; Professor; Pathology; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2002; Project Start 17-AUG-1994; Project End 31-MAY-2004

  Summary: In mammals, there are approximately 100,000 genes which govern the development of an organism. For development to proceed normally, there must be coordinate interaction of tens of thousands of these gene products in any given cell of the being. Beginning with fertilization, precise expression of these gene products is required during embryonic, fetal, postnatal, and adult development. Aberrant synthesis of even one of these gene products can be disastrous - birth defects, cancer, infertility, and even death are all possible when this developmental program is altered. To fully understand these processes in humans, it is necessary to have physiological models that closely mimic developmental events which occur during the creation of a human being. Toward this end, we have chosen the mouse as the mammalian model for our studies. It is now possible to modify the mouse genome to generate strains of mice with precise genetic mutations. Using this technology, our laboratory has created several models which have birth defects. For example, mice with mutations in the activin betaA and follistatin genes die at birth and have **cleft palate,** a common birth defect in humans of unknown etiology. In addition, mice a mutations in the activin receptor type II gene have skeletal and facial abnormalities which mimic the human Pierre-Robin syndrome; human newborns with this syndrome have defects in the mandible, leading to respiratory distress which must be surgically corrected immediately. In this grant proposal, we will utilize these previously created mouse models as well as additional models (i.e., mice lacking activins betaC an betaE) to study this complex signal transduction system. The Specific Aims are: 1) Define the functions of the liver-specific TGF-beta-superfamily members, activins betaC and betaE; 2) Perform an activin betaB "knockin" to attempt a rescue of activin betaA knockout mice; and 3) Study the postnatal functions of follistatin and activin betaA using inducible knockout systems. Future studies using these mice as in vivo mammalian model systems will enable us to more fully understand the interrelated roles of these proteins in mammalian development and physiology.

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

- **Project Title: GENE DISCOVERY FOR CRANIOFACIAL DISORDERS**

  Principal Investigator & Institution: Spritz, Richard A.; Professor and Director; Human Medical Genetics Program; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

  Timing: Fiscal Year 2003; Project Start 18-APR-2003; Project End 31-MAR-2007

  Summary: (provided by applicant): Birth defects affect approximately 5% of all infants in the USA, three-fourths involving the head, face, and oral tissues. The most frequent craniofacial birth defects are orofacial clefts: cleft lip +/- **cleft palate** (CL/P) affects ~1 per 1100 births in the USA, and **cleft palate** ~1 per 1600 births. Orofacial clefts thus represent a considerable public health problem and expense, and most cases cannot now be predicted or prevented. Isolated, "non-syndromic" CL/P (nsCL/P) is the most common craniofacial birth defect, accounting for approximately 70% of all cases of CL/P. nsCL/P is a non-Mendelian, multifactorial disorder, due to multiple genes, each exerting a relatively small effect, interacting with each other and with environmental factors to ultimately result in defective action of specific pathways and genetic networks during fetal craniofacial development. However, few of the genes, and none of the

environmental influences, that contribute to nsCL/P are currently known with certainty. The goal of this proposal is to identify the genes, pathways, and genetic networks that are involved in craniofacial development and that thus represent potential targets for genetic and non-genetic determinants of nsCL/P. Identification of these targets will be necessary to devise therapeutic strategies ultimately aimed at preventing this debilitating and disfiguring birth defect. It is currently very difficult to accurately study gene action during craniofacial development in the human. Accordingly, we plan a careful microarray study of gene expression profiles in the developing face of the mouse, in which genetic background (C57BL/6J), careful timing of fetal age, sampling at numerous timepoints, and analyses of many replicate samples can all be readily achieved. In addition, we plan an analogous study of facial development in mice homozygous for a null knockout allele of the Ski locus, carried on the C57BL/6J background. These Ski -/- mice have an exceedingly high rate of midline facial clefts, providing an invaluable comparison of gene expression during aberrant craniofacial development that, in particular, should identify genetic pathways and networks of the developing facies that are responsive to Ski. For genes that appear of particular importance during facial development, we will identify and validate human SNPs for use in future linkage and association studies of nsCL/P. We will apply state-of-art bioinformatics tools to analyze and interpret the data, all of which we will deposit in appropriate public data repositories.

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- **Project Title: GENE EXPRESSION FUNCTION AND MUTAGENESIS**

  Principal Investigator & Institution: Soriano, Philippe M.; Member; Fred Hutchinson Cancer Research Center Box 19024, 1100 Fairview Ave N Seattle, Wa 98109

  Timing: Fiscal Year 2004; Project Start 01-JAN-1989; Project End 31-DEC-2008

  Summary: (provided by applicant): Platelet derived growth factors (PDGFs) are required for vascular development, cranial and cardiac neural crest cells, somitic mesoderm, extraembryonic lineages and in the kidney. The mechanisms by which they control cell proliferation, survival and migration have been deciphered in cultured cells, but the identity of the target genes that mediate such pleiotropic functions in development and the adult remain unknown. This proposal focuses on identifying PDGF targets using a novel platform, the gene trap array, in which thousands of cDNAs derived from gene trap disrupted loci in ES cells are spotted on DNA arrays. This approach combines all of the power of DNA array technologies with the possibility of readily generating mutant mice from the frozen ES cell stocks. The physiological roles of a subset of regulated genes will be assessed by deriving mutant mice from the trapped ES cell clones. Target genes will be further characterized by establishing if they are specific for one or the other PDGFR and if they are subject to regulation by other signaling pathways. Conditional gene trap vectors will be generated that allow spatio-temporal elimination of gene activity and the generation of allelic series at the trapped loci. The Gene Trap Array will be expanded to 10,000 mutant ES cell clones and genes mutated by these vectors will be identified by sequencing and their identity will be listed on a web-based platform. Critical components of PDGF signaling will be identified in neural crest cells, using two complementary approaches, the gene trap array or gain-of-function gene trap mutagenesis in a PDGFalphaR sensitized background. Gain-of-function alleles that synergize with a PDGFalphaR mutation will be converted to loss of function alleles to study the normal function of the gene. These studies may shed insight on birth defects associated with abnormal neural crest development, such as **cleft palate** or DiGeorge Syndrome.

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- **Project Title: GENE-ENVIORNMENT INTERACTIONS IN FACIAL CLEFTS**

  Principal Investigator & Institution: Christensen, Kaare; Research Professor; University of Southern Denmark Campusvej 55 Odense,

  Timing: Fiscal Year 2003; Project Start 01-MAR-1998; Project End 31-MAY-2007

  Summary: (provided by applicant): Clefts of the lip and/or palate are among the most common and easily diagnosed birth defects, and can provide a model for complex trait analysis. Family and twin studies have clearly indicated a genetic role in the etiology of cleft lip and palate, but environmental components play a major role, as well. The environmental risk factors identified (e.g., medications, alcohol, smoking, nutritional deficiencies) are weak (O.R. < 1.5). Similarly, genetic analysis has not as yet identified any strong single gene as playing a major role in clefting. In the previous funding cycle of this proposal, we were able to analyze a large sample for both case parent triads and case controls for environmental data and molecular analysis. The initial submission took advantage of the cleft population that has been studied in Denmark since the 1930s and which provided an ethnically homogenous population, as well as an extensive historic database to carry out the studies. In this resubmission, we will now partner with parallel efforts underway in Norway, and take advantage of a well-established collaboration between Norway, Denmark and the United States. In addition, we have added a state-of-the-art epidemiologic analytic team based at the National Institutes of Environmental and Health Sciences who are developing new analytic tools to take advantage of the sample sizes available. Finally, advances in molecular technologies--particularly the identification of single nucleotide polymorphisms (SNPs)--have afforded the opportunity to carry out genotyping at an unprecedented level for a group of genes which have a high prior probability of being directly involved in clefting. The combination of these unique resources affords the opportunity to study cleft lip and palate in detail. In this project, we will characterize 50 candidate genes and 150 SNP markers within those genes in a total of 600 case parent triads for both isolated **cleft palate** and cleft lip with or without **cleft palate.** Positive findings from this initial analysis will then be confirmed in a case control analysis using over 800 cases and 2800 controls. Confirmed findings at this stage will then undergo statistical analysis with an emphasis on gene-gene interaction and, eventually, studies of gene-environment interaction. This project will also set the stage for our use of two large cohort studies taking place in Denmark and Norway in which 200,000 consecutive pregnancies will be ascertained, and detailed epidemiologic, environmental, and biological data made available for studies of clefting. This study will provide a new level of understanding for a complex birth defect trait.

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

- **Project Title: GENETIC ANALYSIS OF TBX1 IN EAR DISORDERS**

  Principal Investigator & Institution: Morrow, Bernice E.; Associate Professor of Molecular Genetic; Molecular Genetics; Yeshiva University 500 W 185Th St New York, Ny 10033

  Timing: Fiscal Year 2003; Project Start 01-DEC-2002; Project End 30-NOV-2007

  Summary: (provided by applicant): Velo-cardio-facial syndrome/DiGeorge syndrome (VCFS/DGS) is a congenital anomaly disorder associated with hemizygous 1.5-3 Mb 22ql 1 deletions. Most patients have learning disabilities, craniofacial anomalies, outflow tract heart defects and ear disorders. Over 24 genes lie in the 1.5 Mb interval that is

deleted. The 1.5 Mb region is conserved on mouse chromosome 16. By taking genetics approaches, we recently found that one of the genes, termed Tbxl, a member of the T-box family of transcription factor genes, is a strong candidate for the syndrome in mouse models. We targeted the Tbxl gene for inactivation and found that while hemizygous mice were mildly affected, homozygous mice died in the perinatal period with malformations that were particularly striking in their magnitude. They had **cleft palate,** major cardiovascular defects, no thymus or parathyroid glands and no outer, middle or inner ear. We are interested in determining the role of Tbxl in ear development and disease. Both the otic vesicle epithelium and surrounding periotic mesenchyme interact to form the inner ear. The fact that Tbxl is highly expressed in both tissues, suggests that it might play dual roles in patterning the inner ear. We hypothesize that Tbxl encodes a transcription factor whose dual expression is required for ear development. For Specific Aim 1, we will determine the role of Tbxl in the otic vesicle epithelium and separately in the periotic mesenchyme by generating conditional alleles in the mouse. For Specific Aim 2, we will determine whether Tbxl is a transcriptional activator or repressor and define the Tbxl domains required for transcription factor activity. Two other T-box genes, Tbx2 and Tbx3, are co-expressed in the otic vesicle during development. The basis for Tbxl function may lie in its requirement to form functional homodimers or heterodimers. We will determine whether Tbxl protein can functionally interact with Tbx2 or Tbx3. Many genes required to form the ear have been identified. We will take a candidate gene approach to determine the role of Tbxl in altering the expression of downstream target genes in the ears of mutant mice as Specific Aim 3. By achieving the goals of these specific aims, we will understand the role of Tbxl in normal ear development and disease.

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- **Project Title: GENETIC AND DEVELOPMENTAL ANALYSIS OF MOUSE CLEFT PALATE**

  Principal Investigator & Institution: Maas, Richard L.; Associate Professor and Chief; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2007

  Summary: (provided by applicant): Non-syndromic CP and CL(P) exemplify complex birth defects with both multigenic and environmental contributions. However, relatively little is known about the developmental or genetic basis for orofacial clefting. This may relate to heterogeneity in the combinations of genes that predispose to CP and CL(P), and to constraints imposed by human genetic variation. We suggest that the mouse offers certain advantages for furthering our genetic and molecular understanding of CP and CL(P). Specifically, the large battery of available mouse orofacial clefting mutants provides a unique opportunity to develop a systematic, mechanism-based classification for genes whose function is required for palatogenesis. We posit that mouse clefting mutants can be grouped into specific developmental classes based on the step at which the respective genes act. Moreover, we propose that within each class of mutants, genes that are co-expressed, or that - based on existing functional annotation - can be logically considered to act within a specific pathway, should have a high likelihood of interacting genetically when the respective mutant alleles are compounded. Conversely, genes that reside in different classes should not. In this way, we hope to begin to model the complex inheritance of CP and CL(P). In Aim 1, we will clone the genes for four new recessive mouse clefting mutants generated in our ENU mutagenesis screen. Three mutants, cpo1, ctcp and Ic express a cleft secondary palate, and we have already cloned cpo1, revealing a novel Zn-finger gene. A fourth mutant, clf3, expresses isolated cleft lip.

In Aim 2, we will analyze the mutant phenotypes in comparison with existing mouse clefting mutants to determine the specific developmental step at which each gene acts. Lastly, in Aim 3, we will test specific hypotheses about the relationship between the respective genes and their products. This will involve carefully selected developmental and molecular experiments, and the generation of genetic compound heterozygotes to test whether combinations of the recessive loci identified model the complex inheritance of CP or CL(P). In sum, these experiments should identify new genes involved in orofacial clefting, advance our understanding of the developmental mechanisms involved, integrate the genes into developmental and molecular pathways, and reveal how these loci interact genetically to contribute to orofacial clefting.

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

- **Project Title: GENETIC AND MOLECULAR ANALYSES OF MUTATIONS**

  Principal Investigator & Institution: Brilliant, Murray H.; Professor of Mammalian Genetics; Pediatrics; University of Arizona P O Box 3308 Tucson, Az 857223308

  Timing: Fiscal Year 2002; Project Start 01-JUL-1989; Project End 30-JUN-2003

  Summary: (Adapted from investigator's abstract) This is a competitive renewal for an RO1 in its third funding cycle that requests five years of support to identify and analyze genes uncovered by genetic rearrangements that affect the p gene. Previous work by the applicant has defined two complementation groups -- runty/jerky/sterile (rjs) and **cleft palate** -- which lie proximal and distal to p, respectively. In the previous funding cycle, the applicant identified a very strong candidate for the rjs gene, demonstrated that deletion of the Gabrb3 gene was responsible for **cleft palate,** and, in addition, described an inversion allele, p100H, that disrupts the Sox6 gene and causes an unusual muscle disease reminiscent of Emery-Dreyfuss muscular dystrophy. The current application proposes to extend work in all three areas. The molecular pathogenesis of rjs deficiency will be investigated by further characterization of gene and protein expression, by identification of interacting proteins, and, in collaboration with others, biochemical and/or cell biologic assays of rjs domains that may function in protein ubiquitination and guanine nucleotide exchange. In addition, a loxP-flanked rjs allele will be created to investigate whether the pleiotropic phenotype caused by rjs deficiency reflects the sum of several tissue-specific defects. Preliminary studies suggest that **cleft palate** caused by deficiency for Gabrb3 reflects a requirement outside the central nervous system, pointing to a potentially novel role for GABA signaling during palate morphogenesis. These data will be confirmed by further studies of a Gabrb3 transgene controlled by the neuron-specific enolase promoter. In addition, the sites of Gabrb3 gene and protein expression, and GABA binding sites, will be characterized in non-neuronal tissues with special attention to the developing palate. The pathogenesis of muscle disease caused by the p100H mutation will be investigated by further characterization of a newly recognized Sox6 isoform highly expressed in muscle, by development of myoblast/myocyte cell culture systems from mutant animals, and by Sox6 gene rescue experiments in vivo and/or in vitro. In addition, differential display, cDNA subtraction, and/or gene expression profiling will be used to compare mutant and non-mutant tissues in an attempt to identify Sox6 targets.

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

- **Project Title: GENETIC ETIOLOGY OF NONSYNOMIC CLEFT PALATE**

  Principal Investigator & Institution: Lidral, Andrew C.; Associate Professor; University of Iowa Iowa City, Ia 52242

Timing: Fiscal Year 2002; Project Start 10-JUL-2002; Project End 31-JUL-2002

Summary: Cleft lip and **cleft palate** are common birth defects affecting 1-2/1000 live births. It is apparent that genetic factors contribute significantly to their etiology. Most orofacial clefts are non- syndromic, isolated effects, which can be separated into two different phenotypes: (1) cleft lip with or without **cleft palate** (CL/P) and 2) **cleft palate** only (CPO). Both are genetically complex traits, which has limited the ability to identify disease loci or genes. Previous effects to determine the genetic etiology for non-syndromic clefts have relied on candidate gene approaches with most studies focused on CL/P. The overall objective of this and future projects is to identify disease loci and genes involved in non-syndromic CPO by employing new linkage strategies to study affected relative pairs and extended pedigrees. These approaches, which have yet been applied to CPO, are very powerful in that no prior knowledge about the involved biological processes or inheritance pattern is needed. The specific aim of this project is to ascertain 150 families with multiple members affected with CPO from the Shanghai region of China. An additional 100 CPO patients will be ascertained along with their parents for use in linkage disequilibrium analyses. This will be performed in collaboration with Dr. You-e Liu of the Zhabei Eye Hospital, Shanghai and Dr. Mary Marazita of the **Cleft Palate** Center, Pittsburgh, who have collaborated since **Cleft Palate** Clinic at the University of Pittsburgh Cleft Palate-Craniofacial Center to add to the 45 families already recruited through the efforts of there collaborative investigators. The scope of this project will be to evaluate candidate genes for CPO using both linkage and linkage disequilibrium analyses. The population of Shanghai, China is relatively homogeneous, which a unique quality that increases the power to map a disease loci and also facilitate the transition to physical mapping and gene identification. The strength of this study is the relatively large numbers of affected relative pairs that can be ascertained at multiple sites, thus increasing the overall power for the study to detect loci of even modest effect. It will be through projects such as this one, in which collaborations with researchers world wide have been established to apply a combination of genetic strategies, that disease loci for CPO will be identified. Ultimately, this will further the knowledge of normal and abnormal craniofacial development, such that therapies to prevent CPO can be developed.

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

- **Project Title: GROWTH FACTOR SIGNALING IN MOUSE PALATOGENESIS**

  Principal Investigator & Institution: Chen, Yiping; Associate Professor; Cellular and Molecular Biology; Tulane University of Louisiana New Orleans, La New Orleans, La 70112

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

  Summary: (provided by applicant): **Cleft palate** is one of the most common birth defects in human. Mammalian palatogenesis is a complex and multiple step process, largely depending on the sequential and reciprocal interactions between apposed epithelial and mesenchymal tissues involving diffusible growth factors and homeobox genes. Genetic or environmental interruption at any step of this complex process can result in **cleft palate.** Bone Morphogenetic proteins (BMPs), Sonic hedgehog (Shh), and Fibroblast Growth Factors (FGFs) have been implicated in the formation of many vertebrate organs. However, their potential role in mammalian palatogenesis remains unknown. Our previous studies demonstrated that Msx1 homeobox gene, mutations, which are associated with non-syndromic **cleft palate** and tooth agenesis in human, control a genetic hierarchy involving BMPs and Shh in the regulation of outgrowth of the anterior portion of the secondary palatal shelves. In the anterior portion of developing palatal

shelves, the expression of Bmp4, which is regulated by Msx1 in the mesenchyme, maintains Shh expression in the medial edge epithelium (MEE). Expression of Shh in the MEE is required for the growth of palatal shelves via activation of Bmp2 in palatal mesenchyme. Our preliminary studies also demonstrated a restricted expression of FGFR2 in the posterior palatal mesenchyme, which can respond to FGF signal in terms of gene expression, suggesting that FGF signaling may regulate the development of the posterior portion of the palate. In this application, three specific aims are proposed to further test the regulation and function of the BMP-Shh pathway in anterior palatal development, and to establish a role for FGF signaling in the regulation of posterior palate development. Aim 1 is designed to examine the regulatory mechanism of Shh expression in the MEE by mesenchymal BMP4. The specific type I BMP receptor that is involved in this regulation will also be determined. Transgenic mice will be generated that carry either a dominant-negative BMP receptor-IA transgene driven by the K14 promoter or a constitutively active BMP receptor-IA transgene driven by the Msx1 promoter. In Aim 2, the role of Shh in palate formation will be defined by analyzing Shh conditional knockout mice and transgenic mice overexpressing Shh in the palatal epithelium. It will also test whether ectopic Shh expression in the palatal epithelium of the Msx1 mutants can bypass the requirement for both Msx1 and BMP4 in palatal mesenchyme to restore cell proliferation and rescue **cleft palate.** Lastly, in Aim 3, the role for FGF signaling in palatogenesis will be established by testing FGF's function in the regulation of cell proliferation and survival in vitro by organ culture, and in vivo by analyzing Fgf10 knockout mice that exhibit a **cleft palate.** Our long-term goal is to unveil the molecular mechanisms of mammalian palatogenesis and **cleft palate** formation, which would provide insight for genetic prevention and therapy for human **cleft palate.**

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

- **Project Title: IDENTIFICATION OF DOSAGE SENSITIVE GENES ON 18Q**

  Principal Investigator & Institution: Cody, Jannine D.; Pediatrics; University of Texas Hlth Sci Ctr San Ant 7703 Floyd Curl Dr San Antonio, Tx 78229

  Timing: Fiscal Year 2004; Project Start 14-JAN-2004; Project End 30-NOV-2008

  Summary: (provided by applicant): One of every 180 live-born infants has a chromosome abnormality making it a leading cause of disability. Human genome sequence data now permits the identification of specific genes associated with each aneusomy, the correlation of these genes with specific phenotypes, and ultimately therapeutic options. Toward this end, we have established and sustained a large multidisciplinary team: The Chromosome 18 Clinical Research Center. Herein, we propose a model for identifying the specific gene(s) associated with each phenotypic feature of 18q deletions (dosage sensitive genes). The model may be widely applicable to other chromosome abnormalities. Deletions of 18q are among the most common of the chromosome abnormalities, yet no dosage sensitive genes have been identified whose hemizygosity results in haploinsufficiency and therefore a phenotype. Our goal is to identify dosage sensitive genes on 18q and to characterize the clinical consequences of this hemizygosity. Building on our extensive experience with the chromosome 18 syndromes, we propose to correlate specific key phenotypic features (dysmyelination, growth hormone deficiency, atretic/stenotic ear canals, autism, **cleft palate,** and severe developmental delay) with the deletion of particular regions of chromosome 18q (critical region). To further narrow this critical region to a candidate gene (or genes), we will study karyotypically normal children with a specific phenotype (e.g., dysmyelination) and search for microdeletions in the previously identified critical region on chromosome

18. This strategy has already been used to identity a candidate gene responsible for the dysmyelination phenotype. Sequencing of the candidate gene in the phenotype specific population will identify additional individuals with chromosome 18q based disease. Then, the karyotypically normal child with chromosome 18q based disease will be clinically assessed to determine the spectrum of expressivity. This last step will initiate the process of comprehensively defining the phenotype resulting from deletion or mutation of an individual dosage sensitive gene. Furthermore, it will begin to piece together the genotypic components that combine to generate the full phenotype of a child with an 18q deletion.

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

- **Project Title: INHIBIN/ACTIVIN FAMILY IN HUMAN CRANIFOCIAL DEVELOPMENT**

  Principal Investigator & Institution: Lambert-Messerlian, Geralyn M.; Women and Infants Hospital-Rhode Island 101 Dudley St Providence, Ri 02905

  Timing: Fiscal Year 2002; Project Start 01-MAR-2002; Project End 28-FEB-2004

  Summary: The etiology of craniofacial abnormalities is multi-factorial and defects such as **cleft palate** often occur in the absence of a known cause. Compelling data suggest that inhibin/activin family of proteins is critical for normal craniofacial development and that aberrant production or action of these proteins may have a role in craniofacial defects. Transgenic mice lacking the inhibin/activin betaA gene had severe craniofacial abnormalities that prevented suckling in the pups and led to perinatal death. Knock-out of follistatin also resulted in palate abnormalities, and a subset of mice lacking an activin receptor had skeletal and facial abnormalities similar to that of the human Pierre-Robin syndrome. While activin (beta/beta dimer) was discovered on the basis of its reproductive functions, we now know that this protein, a member of the TGF-beta superfamily, serves as a regulator of growth and differentiations in a variety of cell systems. In particular, activin is critical for mesoderm induction in Xenopus, and activin and follistatin are important in the development and metabolism of bone, a tissue critical for palate formation. Inhibin/activin/follistatin proteins and genes are expressed in a wide spectrum of human fetal tissues. Our preliminary data show that activin protein and activin receptors are present in the developing human fetal palate. Based on these findings, we hypothesize that the inhibin/activin family has a critical role in normal human craniofacial development and that craniofacial malformations can result from deficient production or activity of one or more of these proteins. Since this family has not yet been studied in human craniofacial tissues, the first aim is to elucidate the temporal and regional localization and expression of the inhibin and activin subunits, follistatin and activin receptors throughout normal human craniofacial development using autopsy tissues collected from embryonic through neonatal ages. The second aim is to determine whether alterations in mRNA expression, protein biosynthesis, or protein actions for activin, follistatin or activin receptors are associated with **cleft palate** in humans by comparison with gestational age-matched normal palate tissues. The long term goals of this project are to study the underlying mechanism(s) by which the inhibin/activin family of proteins may lead to craniofacial malformations such as **cleft palate,** and ultimately to devise a prenatal treatment that may prevent or reverse the malformation.

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

- **Project Title: MAPPING NONSYNDROMIC CLEFT LIP AND PALATE GENETIC LOCI**

  Principal Investigator & Institution: Hecht, Jacqueline T.; Professor; Pediatrics; University of Texas Hlth Sci Ctr Houston Box 20036 Houston, Tx 77225

  Timing: Fiscal Year 2003; Project Start 01-APR-1999; Project End 31-MAR-2007

  Summary: (provided by applicant): Nonsyndromic cleft lip with or without **cleft palate** (NSCLP) is one of the five most common birth defects affecting 4,000 newborns per year in the United States. The etiology of NSCLP is complex. Although a number of susceptibility loci have been identified, they are postulated to play only a small etiologic role. The challenge now is to identify the genes that play a major role. A recent study in the mouse suggests that there are major NSCLP loci and that they can be identified. To accomplish this task, it is important to have a defined population and the methodology to detect linkage with and without association. Towards these goals, we have identified and characterized a large sample of multiplex NSCLP families. This unique resource of NSCLP families provides strong evidence that genetic factor(s) play an important role. Using these families, we have positionally identified four new candidate chromosomal regions and confirmed six chromosomal regions from a recent sib-pair analysis study that may contain NSCLP loci. In this continuing work, we will use our unique and large set of multiplex NSCLP families to refine these new candidate regions and test a set of biologically relevant candidate genes. At the same time, we will expand our multiplex families and then conduct a dense 5 cM genome-wide scan to optimize detection of NSCLP genetic loci. Parametric and nonparametric analyzes will incorporate environmental and vitamin exposures and maternal genotype information. Finally all candidate NSCLP genes yielding positive results will be tested in ethnically diverse simplex trios that we are collecting. The results of this study will provide insights into the causes of familial NSCLP and may yield new information about isolated NSCLP. Finally, identification of high-risk genotypes may lead to the development of prevention programs in selected populations and may suggest gene-based prevention strategies.

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

- **Project Title: MELATONIN & SLEEP STUDIES IN CHILDREN W/ DEVELOPMENTAL DISABILITIES**

  Principal Investigator & Institution: Hagerman, Randi; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

  Timing: Fiscal Year 2002

  Summary: This abstract is not available.

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

- **Project Title: MEMBRANE DEFECT IN THE SLO SYNDROME**

  Principal Investigator & Institution: Tulenko, Thomas N.; Professor; Surgery; Thomas Jefferson University Office of Research Administration Philadelphia, Pa 191075587

  Timing: Fiscal Year 2002; Project Start 12-SEP-2002; Project End 30-JUN-2006

  Summary: (provided by applicant): The Smith-Lemli-Opitz (SLOS) syndrome is an often lethal, autosomal recessive birth defect characterized by widespread neurological, skeletal and anatomical abnormalities including **cleft palate** in afflicted subjects. This disorder has been shown to be caused by an inheritable metabolic defect in which the enzyme that catalyzes the final step in cholesterol biosynthesis, DHCR7, is genetically deficient. In SLOS, blood and tissue levels of cholesterol are greatly suppressed while

the levels of the principle precursor to cholesterol synthesis, 7 dehydrocholesterol (7-DHC) are greatly elevated. Because cholesterol is absolutely required for the normal biosynthesis of cell membranes as well as steroid and sex hormones, it is thought that the suppressed cholesterol synthesis in SLOS patients underlies the widespread tissue and organ malformations. While the metabolic defect underlying SLOS has been defined, its impact on cell function has not been determined. In skin fibroblasts obtained from SLOS patients, we have generated preliminary data demonstrating that membrane calcium permeability is markedly augmented while membrane-bound Na+/7K+ATPase activity, folate uptake and IP3 signaling is markedly suppressed. Furthermore, employing X-ray diffraction analyses in synthetic membranes prepared to mimic SLOS membranes, we observed a highly atypical membrane structure. We have developed the hypothesis that in SLOS patients, the deficiency in cholesterol biosynthesis leads to the production of cell membranes that are defective in their composition, dynamics and function, and that this membrane defect contributes to the cellular pathobiology in these patients. In this study, Aim 1 will determine whether defects exist in composition, structure and fluidity of the cell plasma membrane of skin fibroblasts obtained from SLOS patients and DHCR7 transgene knockout (k/o) mice. Aim 2 will determine whether these membrane defects correlate with impaired membrane function (folate uptake, Ca++ permeability, Na+/K+ATPase activity and IP3 signaling) and cell proliferation. Aim 3 will determine the degree to which cell and membrane functions can be corrected by restoring the membrane sterols back to normal levels. This project employs biophysical, biochemical and cell biology approaches to study fibroblasts obtained from SLOS patients and DHCR7 k/o mice in an attempt to shed light on the cellular basis underlying this profoundly debilitating disease which has no cure. By defining the membrane defects in SLOS we will advance our understanding of cell and molecular basis of this disease. In addition, we expect to validate the DHCR7 k/o mouse model of SLOS and thereby provide greater opportunity for us and others to study SLOS in the hope of providing clinical relief to patients faced with this disease.

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

- **Project Title: MINNESOTA DENTIST SCIENTIST AWARD PROGRAM**

  Principal Investigator & Institution: Herzberg, Mark C.; Professor; Oral Sciences; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

  Timing: Fiscal Year 2002; Project Start 01-JUL-1990; Project End 30-JUN-2003

  Summary: The University of Minnesota aims to recruit dentists for a program of didactic and advanced basic research training and advanced clinical training. In the Minnesota Dentist-Scientist Award (DSA) program, a Ph.D. in Oral Biology will formalize didactic and research training. DSA fellows will select one of five research training areas (RTAs) as defined by dental research needs and Minnesota faculty strengths: Microbiology and Immunology; Biophysical Sciences; Neurosciences; Pathobiology; and Mineralized and Connective Tissues. A graduate faculty dental scientist from an RTA will be a mentor to the DSA fellow. The application highlights 37 potential mentors, of whom 22 are appointed in the School of Dentistry. The Ph.D. program will be integrated by calendar, leadership, organizational structure, mentor responsibility, and philosophy with ongoing NIH/NIDR postdoctoral research training programs at Minnesota and the DSA fellow's advanced clinical training (ACT) program. There are 10 ACT programs, including four innovative disciplines particularly suited for academic and research careers. The Minnesota ACT programs are Periodontology, Pediatric Dentistry, Oral Pathology, Endodontics, Prosthodontics, Orthodontics, Operative Dentistry, Oral Health Services for Older Adults (OHSOA), Temporomandibular Joint and Craniofacial Pain

(TMJ-CP), and **Cleft Palate,** Maxillofacial Therapy and Craniofacial Anomalies (CP-MT-CA). The ACT programs included by the DSA Working Group have strong academic records. Many clinical faculty are also Graduate Faculty of the University with recognized research and scholarly accomplishment. The administration of the Minnesota DSA program will ensure that state-of-the-art training is provided to outstanding DSA fellows. The program will be directed by Mark C. Herzberg, D.D.S., Ph.D. An associate director, DSA Advisory Committee and an External Advisory Committee will provide administrative guidance, support, and program analysis. In summary, the Minnesota DSA program will provide highly trained dentist-- scientists to work at the leading-edge of basic and clinical dental research.

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

- **Project Title: MOLECULAR ASPECTS OF VELO-CARDIO-FACIAL SYNDROME**

  Principal Investigator & Institution: Kucherlapati, Raju M.; Professor; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 05-DEC-1996; Project End 30-NOV-2004

  Summary: The goal of this project grant application is to understand the molecular basis of vole-cardio-facial syndrome (VCFS). This human syndrome has an incidence that is grater than 1 in 5,000 live births and is characterized by defects involving several organ and tissue systems. The children have **cleft palate,** pharyngeal insufficiency, cardiac and conotruncal abnormalities that result from thymic asplasia and hypoparathyroidism. As the children grow, they exhibit learning disabilities and older individuals develop psychiatric illness. Because several of the affected organs are derived from neural crest and from the pharyngeal pouches, it was postulated that at least some of the phenotypes are the result of a developmental field defect. A large proportion of VCFS patients have an interstitial deletion of chromosome 22 suggests that haploinsufficiency of one or more genes in the deleted region causes the disorder. To understand the molecular basis of this disorder, we constructed a high resolution physical map of the 22q11 region in the form of overlapping yeast artificial chromosomes and bacterial clones, mapped highly polymorphic markers and used them to de3fine a commonly deleted or a "critical" region. Twenty genes that fall in the critical region have been identified by us and others. During the past two years, we have defined the mechanism for deletions in these patients, examined the expression patterns of several genes and generated mice with mutations in a number of genes. We now proposed to extend these studies. In Project 1, we will examine the precise DNA sequences that undergo germline rearrangement that lead to deletions and will seek cis elements that might make the chromosomes prone to rearrangement. We will also isolate cDNAs in the region common deleted in VCFS patients and conduct genotype-phenotype correlations. In Project 2, we propose a new method to examine changes in patterns of gene expression in embryos from several knockout mice we generated and others that are VCFS phenocopies. We expect that these studies will lead to identification of genes whose haploinsufficiency leads to phenotypes associated with VCFS. In Project 3, we propose to produce mice withy mutations in mutations in Ufd11 and Tbx, two genes that are candidates for VCFS phenotypes. We also propose to produce and analyze deletions in mice that correspond to those seen in human patients. Such mice may provide models for VCFS, leading to a detailed understanding of the molecular basis of VCFS.

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

- **Project Title: MOLECULAR GENETIC ANALYSIS OF CRANIOFACIAL DEVELOPMENT**

  Principal Investigator & Institution: Jiang, Rulang; Assistant Professor; Eastman Dentistry; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

  Timing: Fiscal Year 2002; Project Start 01-APR-2000; Project End 31-MAR-2005

  Summary: (adapted from the Investigator's abstract): The long-term goal of the proposed research is to understand the molecular genetic mechanisms underlying craniofacial development. Craniofacial malformations, including **cleft palate,** occur with a frequency of 1 in 600 live births in the United States. Despite the prevalence of **cleft palate** in the human population, the pathogenic processes that lead to **cleft palate** are not well understood. Mice with mutations that cause **cleft palate** provide excellent animal models to determine the molecular mechanisms underlying normal palate development and **cleft palate** formation. A targeted mutation in the mouse Jag2 gene causes complete penetrance of **cleft palate.** Jag2 encodes a cell surface ligand for the Notch family receptors and is expressed throughout the oral epithelium during palate development. This proposal addresses the following questions: (1) what specific cellular and molecular processes during palate development depend on Jag2 function? (2) which Notch receptor(s) mediates Jag2 function in palate development? (3) what molecules act in the Jag2-Notch signaling pathway to regulate palate development? A combination of molecular, genetic, and embryological approaches will be used to find answers to these questions. These studies will provide insights into molecular and cellular mechanisms governing palate development and will greatly extend current understanding of the mammalian Notch signaling pathway.

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

- **Project Title: MORPHOGENESIS OF CRANIAL NEURAL CREST CELLS**

  Principal Investigator & Institution: Roman, Laura M.; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2002

  Summary: Craniofacial malformations constitute one of the major group of congenital defects in newborn human infants. The formation of the anterior aspect of the vertebrate embryo is a complex process for which we have few molecular details, especially regarding the contribution of the neural crest (NC). The neural crest is a transient structure composed of cells that migrate extensively throughout the embryo and contribute to a number of organs. The control of crest cell morphogenesis is critical to the embryo, in as much as abnormal neural crest migration or proliferation result sin a number of serious human disorders ranging from **cleft palate,** to frontonasal dysplasia. The cranial malformations observed in children exposed in utero to 13-cis retinoic acid (RA) or excess alcohol are a consequence of the drugs' effect on some aspect of crest cell morphogenesis. The long term goal of the laboratory is to define the factors controlling normal craniofacial development and to elucidate the mechanism and to elucidate the mechanism(s) by which retinoic acid (RA) and ethanol affect these processes. While other vertebrate systems have provided insight into some of the key steps in crest cell morphogenesis, these studies have been limited by the complexities of these organisms and inaccessibility of the embryonic tissues. We propose to use zebrafish as a model to study the role of the NC in craniofacial development. Since the embryo is transparent, the movement of individual cells can be visualized in real time. Like humans, the formation of the anterior structures of the zebrafish embryo is sensitive to teratogens like RA and ethanol. The studies outlined in this proposal focus on the transcription

factor AP-2, which has been shown to be expressed in NC cell populations. Which make major contributions to the developing head in human, mouse and chick. The specific aims of this proposal are: 1) To establish AP-2 as a marker for subsets of NC cells in zebrafish, and examine how exposure to RA and ethanol affect the morphogenesis of the AP-2+ crest cell populations; 2) To examine the role of AP-2 in craniofacial development by altering the expression of this gene product; 3) To follow the morphogenesis of AP-2+ cell populations in the living embryo. Through the use of this model system we will be able to gain significant insights into the dynamic movements of cranial NC cells during embryogenesis. These studies will have a major impact on our understanding of the hierarchy of cell movements and interactions critical for the normal formation of the head and facial structures.

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- **Project Title: NON-SYNDROMIC CLEFT PALATE IN MICE**

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

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2005

  Summary: (provided by applicant): Development of the mammalian secondary palate is a complex and critical process that in man can be easily perturbed leading to the common and distressing birth defect, **cleft palate** (CP). Clefts of the primary and/or secondary palates are consistently included among the more common congenital anomalies occurring in man. Even though the combination of cleft lip with/or without **cleft palate** (CLIP) is more commonly seen, isolated CP can account for approximately one-third of the documented cases. Isolated CP is considered to be an etiologically heterogeneous trait with an important genetic contribution. While CP can be associated with more that 350 characterized disorders, more than 50% of cases of CP occur as isolated (sporadic) and thought to be free of other anomalies (non-syndromic). Our long-term objectives focus on identifying genetic determinants that directly and/or indirectly (i.e. genetic susceptibility and multifactorial causes) contribute to the failure of mammalian secondary palate formation (using animal models) and to better understand the roles that these genes play at the molecular level during normal secondary palate formation. Similarities in palate development between humans and mice have allowed the later to be an important model organism for studying normal and defective palatogenesis. Transgene insertion mutagenesis can facilitate the identification of developmentally important genes through non-homologous disruption of endogenous genes. We have been investigating four separate lines of transgenic mice that develop autosomal recessive nonsyndromic **cleft palate** involving a least three distinct loci that localize to chromosomes 3 and 4. The focus of this research project is to characterize the interval of genomic DNA disrupted by these transgene insertions as a prelude to identifying the disrupted genes responsible for **cleft palate** in these mice.

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

- **Project Title: NUTRIENT BIOMARKERS, GENES AND OROFACIAL CLEFTS**

  Principal Investigator & Institution: Munger, Ronald G.; Associate Professor; Nutrition and Food Sciences; Utah State University 1415 Old Main Hill Logan, Ut 843221415

  Timing: Fiscal Year 2002; Project Start 23-JUN-2000; Project End 31-MAY-2005

  Summary: (Adapted from the Applicant's Description) Orofacial clefts are among the most common birth defects in the world yet little is known about their major causes and

regional differences in occurrence. In our previous studies in the Philippines we recently found biochemical evidence that poor vitamin B-6 and folic acid levels of mothers are independently associated with increased risks of clefting and that the MTHFR C677T mutation is associated with a reduced risk of clefting. We propose to elaborate these methods for studying nutrient-gene interactions and apply them in a population-based case- control study of orofacial clefts in Utah with the following specific aims: (1) Children with orofacial clefts (n = 686) will be ascertained by the state- wide Utah birth defects registry and their mothers will be recruited as case participants; (2) Children without clefts (n= 686) will be randomly selected from Utah birth certificates and their mothers wIll be recruited as control participants; (3) Data will be collected on dietary patterns, smoking, alcohol use and other exposures using telephone-based interviews and mailed questionnaires; (4) Venous blood samples will be drawn from mothers, rapidly processed, and assayed for biochemical indicators of vitamin B-6 and folate status; (5) DNA from mothers, children, and fathers will be prepared and genotyped for polymorphic genetic markers related to vitamin B-6 and folate metabolism. The following hypotheses will be addressed: (1) Poor maternal vitamin B-6 status is independently associated with increased risk of orofacial clefts; (2) Poor maternal folate status is independently associated with increased risk of orofacial clefts; (3) The MTHFR C677T allele is associated with a reduced risk of clefting. In addition the association between allelic variants of other folate- and vitamin B-6-related genetic markers and the risk of orofacial clefts will be examined; (4) The nutrients and candidate genes mentioned above interact, additively or multiplicatively, to increase the risk of orofacial clefting. Our multidisciplinary study of maternal nutrition and risk of clefting in the context of genes related to metabolic pathways may lead to a better understanding of the causes and prevention of orofacial clefts.

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

- **Project Title: ORAL FACIAL CLEFT FAMILIES--PHENOTYPE AND GENETICS**

  Principal Investigator & Institution: Marazita, Mary L.; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002

  Summary: Oral-facial clefts, particularly cleft lip with or without **cleft palate** (CL/P), are a major public health problem, affecting one in every 500- 1000 births worldwide. Therefore, many research groups have attempted to identify genetic loci contributing to the etiology of CL/P, with limited success to date. There have been several allelic associations identified in European Caucasian populations, a few potentially linked markers; however, these results have not been consistent across study populations. It appears that the genetic contribution to the etiology of oral-facial clefting is complex, possibly heterogeneous, or possibly due to interacting effects of multiple loci. A possible impediment to identifying loci for clefting is that the cleft itself is unlikely to be the proximate phenotype coded by the etiologic gene or genes. There is increasing evidence that developmental asymmetry effects may contribute to the etiology of oral-facial clefts. If we can more accurately identify the phenotype that is segregating at a genetic level in these families, then gene mapping and association studies will be more successful. Furthermore, it we can identify unaffected individuals who are likely to carrying cleft genes (e.g. individuals with sub-clinical phenotypic expression), then recurrence risk calculation and genetic counseling for this common birth defect will be vastly improved. The goal of this project is to investigate phenotypic features in multiplex kindreds (i.e. with 2 or more affecteds) ascertained through CL/P individuals served by the University of Pittsburgh Cleft Palate- Craniofacial Center. The specific features that will

be investigated included: handedness, craniofacial measurements, asymmetry (based on dermatoglyphic patterns and craniofacial measurements), and anatomy of the orbicularis oris muscle. These features will be evaluated in each member of the multiplex kindreds. Each individual feature will be analyzed, as well as composite traits composed of two or more features. Statistical genetic methods will be used to investigate the segregation patterns of each trait in the sample of kindreds. In addition, a sample of controls with no known family history of clefting will be evaluated for the same phenotypic features in order to compare to the unaffected relatives (of cleft individuals). DNA will be obtained from all study participants in order to investigate a number of loci that have shown linkage and/or association with CL/P in other studies. These loci are located in specific regions of chromosomes 1, 2, 4, 6, 17 and 19.

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

- **Project Title: OUTCOME MEASURES FOR CRANIOFACIAL ANOMALIES**

  Principal Investigator & Institution: Vargervik, Karin; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002

  Summary: A multi-center project titled: "Registry of Craniofacial Treatment Outcomes," (PI Betty Jane Philips) has been funded by NIDR for the period 01/01/98 through 12/31/02. UCSF Center for Craniofacial Anomalies is one of the ten centers to serve as test sites for the measures as they are developed by the Clinical Outcomes Research Council (COR Council). Dr. Karin Vargervik, Director of the UCSF Center for Craniofacial Anomalies is a member of the COR Council and is one of three members to develop the alveolar bone graft surgery and orthodontic outcomes measures. All measures developed by the COR will be tested in the participating centers and modified as necessary before distribution to all interested **Cleft Palate** and Craniofacial Centers. The aims of the overall project are: 1) development of Craniofacial Registry for collection of clinical outcome data, 2) development of researched clinical outcome data, 2) development of researched clinical outcome measures, 3) introduction of researched measures for widespread (national) collection of data, 4) promotion of internal (self) assessment, by craniofacial teams, based on comparison of their performance with aggregate data, 5) assessment of changes in aggregate data as teams take actions to improve outcomes. Procedures include: 1) design of multiple outcome measures, 2) clinical evaluation of outcome measures, 3) widespread data collection using the researched outcome measures, 4) transfer of the data on clinical outcomes to a Craniofacial Registry, 5) analysis and reporting of aggregate, 6) comparative analysis of outcome performances of interdisciplinary craniofacial teams, 7) report to the Registry of actions taken to improve clinical outcomes, 8) continued collection and transfer of data, 9) assessment of changes in data over time. An environment for the continuing evaluation of craniofacial healthcare outcomes will be created by the development of this Registry and the use of reliable, validated research outcome measures. The UCSF Center for Craniofacial Anomalies is also developing a shared data base for craniofacial anomalies with the Craniofacial Center at Stanford University. It is expected that by being able to pool data and share information we will learn more about effects of treatment in various types of craniofacial birth defects. Ongoing interactions already exist between the clinical and basic scientists to further knowledge, health and potentially prevention.

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

- **Project Title: OUTCOMES OF FURLOW&CONVENTIONAL PALATOPLASTY PROCEDURES**

  Principal Investigator & Institution: Havlik, Robert J.; Surgery; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, in 462025167

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

  Summary: (provided by applicant): This clinical trial planning grant is to design a multi-center, multi-disciplinary prospectively randomized trial to evaluate the outcomes following two **cleft palate** repair techniques--Furlow double-Z palatoplasty (Double Z) and intra-velar veloplasty (IVV). The specific aims of the study are to determine if the primary endpoints of the occurrence of oro-nasal fistulae and the rate of velopharyngeal insufficiently of children undergoing double Z or IVV palatoplasty at 10-12 months of age are the same. It is also believed that cleft type and cleft width may influence these primary endpoints, a series of specific measurements of palatal architecture will be made at the time of palatal repair. Secondary endpoints will be to determine if the occurrence of oro-nasal fistulae or velopharyngeal competence differs as a result of any of these architectural parameters in the two techniques of palatal repair. Patients will be recruited from four major referral sites: Riley Hospital for Children, Children's Medical Center of Akron, Mott Children's Hospital and Children's Mercy Hospital in Kansas City. Total planned enrollment in the trial is 300 cleft patients over three years. Prior to surgery, appropriate screens will be performed to exclude patients with cognitive delay, sensori-neuronal hearing loss, or neuromuscular disorders. All non-syndromic patients with **cleft palate,** with or without cleft lip, will be offered participation in the trial. Audiology testing will be performed throughout the study to minimize the influence of hearing loss upon the data. A speech-language assessment will be performed at nine months of age, and follow-up speech language assessments will be at six-month intervals until 36 months of age, and on an annual basis thereafter until six years of age, or until secondary surgical management is recommended. In addition, a master tape at the 48-month visit will be sent to five independent speech-language pathologists for evaluation in a blinded fashion. Velopharyngeal assessment will be made using nasometry management and analysis will be performed through a separate data center. There are no randomized controlled trials published that compare these techniques of double Z or IVV, and, furthermore, there have been very few randomized trials published in cleft studies, despite this being the third most common birth defect. In addition, there have been no studies on the palatal architecture parameters and their influence upon oronasal fistulae and velopharyngeal competence that have been published.

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

- **Project Title: PREVENTION OF NEURAL TUBE DEFECTS BY IMMUNE STIMULATION**

  Principal Investigator & Institution: Hrubec, Theresa C.; Biomedical Scis/Pathobiology; Virginia Polytechnic Inst and St Univ 460 Turner Street, Suite 306 Blacksburg, Va 24060

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-JUL-2008

  Summary: (provided by applicant): Dr. Terry Hrubec received the D.V.M. and Ph.D. degrees and is embarking on a research career. She is a highly motivated scientist who wishes to make a career shift from clinical pathology and immunology of aquatic species to research in mammalian cellular and molecular immunology. This award would offer Dr. Hrubec an opportunity to strengthen and expand research skills by affording training in molecular mechanisms of developmental abnormalities and using animal

models of human disease. The proposed research investigates the mechanism by which maternal immune stimulation prevents valproic acid (VA) induced birth defects. VA, a drug commonly used to treat epilepsy, is teratogenic and induces neural tube defects (NTDs) in one to two percent of exposed fetuses at a rate 20 times higher than in the general population. In what the investigators feel is paradigm-changing work, data from the investigators' laboratory have conclusively demonstrated that non-specific activation of the maternal immune system in rodents can dramatically reduce a variety of chemical-induced birth defects, including VA induced NTDs. Additionally, the investigators have shown that such maternal immune stimulation normalizes teratogen-altered expression of a few selected fetal cell-cycle/apoptotic regulatory genes in urethane-induced **cleft palate.** A more focused examination of altered gene expression in VA induced NTDs is now logical. Specifically, the investigators will test the hypotheses that: 1) VA affects the expression of genes regulating neural tube development, and that maternal immune stimulation normalizes gene expression through regulatory proteins (cytokines) secreted by activated immune cells; and 2) folic acid supplementation protects against NTDs by cytokine-related mechanisms which may in part be similar to that resulting after maternal immune stimulation. These studies are expected to significantly increase the investigators' understanding of genetic mechanisms by which maternal immune modulation reduces this specific birth defect. Clearly, this research is of importance to human health, as determining the mechanisms involved will improve the understanding of this disorder leading to a prevention or cure. This research will be conducted under the guidance of Drs. Steven Holladay and Ansar Ahmed of the Virginia-Maryland Regional College of Veterinary Medicine at the VPISU, and will offer excellent training and career development for Dr. Hrubec.

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- **Project Title: REGISTRY OF CRANIOFACIAL TREATMENT OUTCOMES**

  Principal Investigator & Institution: Philips, Betty J.; Dental Ecology; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 01-JAN-1998; Project End 31-DEC-2003

  Summary: The purpose of this project is to promote improvement in craniofacial health care outcomes. This study addresses two hypotheses: 1) tha significant discrepancies occurring in the outcomes of craniofacial health wil be identified when treatment outcomes of health care providers are compared an when the outcomes are compared with those suggested by published research and professional papers, and 2) that identification of discrepancies in craniofacial health care, coupled with actions taken by craniofacial teams, will result in improvement of health care outcomes. The aims of this project are: 1) development of a Craniofacial Registry for collection of clinical outcome date, 2) development of researched clinical outcome measures, 3) introduction of researched measures for widespread (national) data collection, 4) promotion of internal (self) assessment by craniofacial teams based on comparison of their performance with aggregate data, and 5) assessment of changes in aggregate data as teams take actions to improve outcomes. Procedure include: 1) design of multiple outcome measures, 2) clinical evaluation of outcome measures, 3) widespread data collection using the researched outcome measures, 4) transfer of the data on clinical outcomes to a Craniofacial Registry, 5) analysis and reporting of aggregate data, 6) comparative analysis of outcome performance of craniofacial teams, 7) report to the Registry of actions taken to improve clinical outcomes, 8) continued collection and transfer of data, and 9) assessment of changes in data over time.

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

- **Project Title: SEARCHING FOR SUSCEPTIBILITY GENES FOR ORAL CLEFTS**

  Principal Investigator & Institution: Beaty, Terri H.; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2002

  Summary: Oral clefts are complex and heterogenous birth defects, and genetic factors are clearly important in their etiology. It has proven difficult, however, to map susceptibility genes through linkage studies. We have been involved in family studies of oral clefts for some time, and have accumulated a number of multiplex families (i.e., those ascertained through two or more probands with an oral cleft) suitable for linkage analysis. As part of the Comprehensive Center for Oral Health Research, we propose to use multiplex families ascertained from four collaborating centers (Mid-Atlantic region of the U.S., Mexico City, Buenos Aries and Prague) to conduct a genome wide search for susceptibility genes. Recent advances in technical methods now make it possible to genotype large numbers of markers on individuals in multiplex families and recent statistical advances make it easier to test for linkage heterogeneity when mapping a complex disorder such as oral clefts. The specific aims of this study are: 1) To conduct a genome wide search for susceptibility loci using multiplex families ascertained from our collaborating centers: Mid-Atlantic, Mexico City, Buenos Aires, and Prague. This mapping effort will focus on efforts to detect linkage and test for linkage heterogeneity, both among families drawn from different populations and within samples of families from a single population. Admixture tests for linkage heterogeneity and conditional approaches for identifying linkage from multiple markers will be employed. 2) To fine map chromosomal region suggesting linkage using these same individuals to identify variant alleles that could be responsible for oral clefting. Results of this study should yield a better understanding of the gene or genes contributing to risk of oral clefts and may suggest strategies for either preventing these birth defects or for identifying individuals at highest risk.

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- **Project Title: SKELETAL MUSCLE STEM CELLS FOR TISSUE REPAIR**

  Principal Investigator & Institution: Kramer, Randall H.; Professor; Stomatology; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

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

  Summary: (provided by applicant): A major problem confronting craniofacial repair is the difficulty in restoring soft-tissue function and contour in patients with anomalies including hemifacial microsomia, unilateral clefts of lips and palate as well as defects in the TMJ. In particular, repair of skeletal muscle defects is limited by difficulty in its transplantation and survival. A logical approach is to use existing population of muscle satellite cells which are quiescent undifferentiated precursors found beneath the basement membrane of mature muscle fibers. Following injury, activated satellite cells regenerate muscle after initiating a differentiation program whereby they migrate along laminin-rich basement membrane, proliferate, differentiate, and integrate with preexisting myofibers. Recent evidence supports the notion that satellite cells are heterogeneous and have stem cell potential. We have shown that the laminin-binding alpha 7 integrin, which is important for myoblast migration, is expressed on a subset of satellite cells and is upregulated in terminally differentiated myotubes. In this application, we propose to examine the potential of using alpha 7-positive human satellite cells for direct repair of muscle defects. We will explore the hypothesis that alpha 7 expressing satellite cells are pluripotent stem cells capable of regenerating

skeletal muscle and other tissue such as bone. The proposal represents three aims. In aim 1 we will characterize human muscle-derived satellite cells and correlate expression of alpha 7 integrin with their differentiation potential for skeletal muscle and other tissue lineages. Aim 2 will determine the expression and function of the alpha 7 integrin during human skeletal muscle development. Aim 3 is focused on the use of alpha 7-expressing human skeletal muscle stem cells to engineer in vitro three-dimensional skeletal muscle myofibers. These studies will form the basis for strategies that target the mechanical reintegration of regenerating myotubes to repair orofacial muscle structures using adult skeletal muscle stem cells.

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- **Project Title: SNP DISCOVERY AND ANALYSIS IN CRANIOFACIAL BIRTH DEFECTS**

  Principal Investigator & Institution: Scott, Alan F.; Director; Medicine; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2002; Project Start 01-MAY-2000; Project End 30-APR-2005

  Summary: (Adapted from the Applicant's Description): This application proposes to locate single nucleotide polymorphisms SNPs using high throughput sequencing of genomic PCR products amplified from genes with demonstrated or presumed relevance to human birth defects. High throughput screening for this panel of SNPs will be applied first to a well characterized set of parent- offspring trios ascertained through a case with non-syndromic oral-facial clefts (OFC), including cleft lip with or without **cleft palate** (CLIP) and **cleft palate** (CP) using a high-throughput screening process, and second to patients with non-syndromic craniosynostosis. These case-parent trios are drawn from separate studies of oral clefts or craniosynostosis designed to identify genes involved in the etiology of this common group of birth defects and test for possible interaction with environmental exposures. The case- parent trio design proposed here tests for linkage in the presence of linkage disequilibrium, and the availability of these DNA samples on a large number of case-parent trios will allow immediate tests for the SNP markers developed as part of this proposal. Following the OFC study the investigators will extend SNP screening to a collection of craniosynostosis patients and their parents from a previous study conducted by the investigators and from the Centers of Birth Defect Research and Prevention sponsored by the Centers for Disease Control (CDC).

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- **Project Title: SPEECH AND RESPIRATORY AERODYNAMICS IN CLEFT PALATE**

  Principal Investigator & Institution: Zajac, David J.; Associate Professor; Dental Ecology; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 01-JAN-1993; Project End 31-MAR-2004

  Summary: (adapted from the Investigator's abstract): The role of the respiratory and laryngeal systems in the generation and regulation of aerodynamic characteristics of speech in individuals with and without **cleft palate** will be explored in three related studies. The specific aims include the determination of (i) lung volume levels used to initiate and terminate speech production, (ii) the limits of the respiratory system to respond to sudden venting of intraoral air pressure during production of bilabial stop consonants, and (iii) the possible role of respiratory and laryngeal reflexes in the regulation of oral air pressure. The three studies are linked theoretically to the

hypothesis that speakers employ both volitional and non-volitional strategies to regulate the aerodynamic substrates of speech production. The first study will determine respiratory lung volume levels of children with **cleft palate** and various degrees of oral-nasal coupling as compared to control speakers. This study will directly test the hypothesis that children with velopharyngeal inadequacy (VPI) use increased respiratory effort as a compensatory strategy. Relationships among variables such as lung volume levels, speaking intensity, and nasal air emission will be determined. The second study will discern the limits of the respiratory system in maintaining adequate oral air pressures in response to sudden and unexpected pressure venting in speakers both with and without **cleft palate.** A newly developed valve will be employed to precisely control the magnitude and timing of pressure perturbations. The rate and maximum levels of pressure recovery following perturbation will be examined relative to cleft status, age, and lung volume levels of the speakers. The third study will attempt to elicit laryngeal reflexes from non-cleft speakers in response to pressure venting. The methodology of the second study will be combined with electromyographic (EMG) recordings from the levator veli palatini (LVP) and posterior cricoarytenoid (PCA) muscles. Anticipated changes in PCA and/or LVP activity in response to pressure venting will be interpreted relative to theories of pressure regulation. These studies are a logical extension of the Principal Investigator's First Award (R29-DE10175). The proposed studies are expected to provide new insights into the respiratory and laryngeal motor control strategies employed by speakers both with and without **cleft palate.** The information obtained from these studies will be instrumental in defining normal aspects of speech aerodynamics. In addition, this information may facilitate the diagnosis and management of individuals with VPI. It is possible, for example, that therapeutic techniques may be developed that incorporate specific respiratory strategies employed by speakers with **cleft palate** who exhibit acceptable speech characteristics.

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- **Project Title: STRUCTURE, LOCALIZATION AND CLONING OF CHANNELS**

  Principal Investigator & Institution: Schwarz, Thomas L.; Associate Professor; Children's Hospital (Boston) Boston, Ma 021155737

  Timing: Fiscal Year 2002; Project Start 01-JUL-1989; Project End 31-MAY-2004

  Summary: This abstract is not available.

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

- **Project Title: SURFACE INTEGRINS AND NEURAL CREST MIGRATION**

  Principal Investigator & Institution: Strachan, Lauren R.; Neurobiology and Anatomy; University of Utah Salt Lake City, Ut 84102

  Timing: Fiscal Year 2002; Project Start 01-MAY-2002

  Summary: (provided by applicant): Cell migration plays a pivotal role in the development of the nervous system. One of the most striking examples of extensive cell movement is exhibited by the neural crest, a transient cell population that travels long distances, interacts with diverse tissues, and gives rise to an impressive array of derivatives. Failure of neural crest migration contributes to craniofacial malformations such as **cleft palate,** clinical syndromes such as Waardenburg's, and numerous developmental abnormalities of the central, peripheral, auditory, and enteric nervous systems. The extensive migration of the neural crest is highly unusual. Although the migration pathways and ultimate cell fates of neural crest cells are well understood, the mechanisms of migration have largely been overlooked. Most embryonic and adult cell

types migrate only under very specific conditions in vitro, and in a correspondingly restricted number of tissues in vivo. There is considerable evidence that the adhesion of neural crest cells to the extracellular matrix (ECM) is mediated by the integrin family of receptors; however the mechanism by which these cells modulate their integrin-mediated adhesion in order to migrate through changing environments is unknown. Recently, we have demonstrated that avian neural crest cells can adapt to and migrate efficiently on a wide range of ECM concentrations in vitro. Interestingly, the extent of adaptation varies along the anterior/posterior (A/P) axis suggesting that differences in integrin regulation may contribute to differences in neural crest migration that thereafter act to restrict developmental potential. Therefore, the experiments outlined in this proposal intend to examine two mechanisms of neural crest migration by (1) determining whether neural crest cells endocytose integrin receptors in order to regulate their surface ECM receptor levels, and (2) determining how integrin-mediated adhesion regulates the activity of Rho GTPases in migrating neural crest cells. These studies will advance our understanding of the mechanisms of neural crest migration and will help to clarify how these cells contribute to the normal development of the nervous system.

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

- **Project Title: SUSCEPTIBLE GENOTYPES**

  Principal Investigator & Institution: Finnell, Richard H.; Professor and Director; Texas A&M University System College Station, Tx 778433578

  Timing: Fiscal Year 2002

  Summary: This proposed research program will investigate genetic susceptibility to environmentally-induced orofacial clefts (ORFs) and neural tube defects (NTDs) using two transgenic mouse models. These two common human congenital defects are considered to be multi-factorial traits, having both a significant genetic and environmental component to their etiology. Given the complex pathophysiology of palatal and neural tube closure, the objective of the proposed research program is to utilize recently developed knock out mouse models lacking either a functional folate binding protein receptor (FBP-1) or a functional Ah receptor with which to test critical hypotheses concerning the role of susceptible genotypes on the development of environmentally-induced congenital malformations. Using the FBP-1 mice we will directly test the hypothesis that elevated levels of homocysteine cause OFCs and/or NTDs in the absence of folate depletion, especially when the embryo is exposed in utero to environmental toxicants. We intend to examine the morphological, biochemical and cellular processes that are compromised within embryos by either the absence of sufficient folate molecules or an increased exposure to high levels of homocysteine, as well as determining those processes that are aided by maternal folic acid supplementation. This include well-defined studies on the impact of the model compounds interacting with embryonic genotypes on cellular proliferation and/or cell death in the developing caraniofacies and neural tube. Additionally, the aryl hydrocarbon receptor (AhR) knockout mouse, which are resistant to aromatic hydrocarbon (TCDD) toxicity, will be similarly used to examine the genetic susceptibility to environmentally-induced birth defects using model environmental contaminants widely found in Texas' Rio Grande Valley as well as in the immediate environs of Sumqayit, Azerbaijan.

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

- **Project Title: SYNDROMIC CARDIAC OUTFLOW TRACT DEFECTS**

  Principal Investigator & Institution: Srivastava, Deepak; Associate Professor; Pediatrics; University of Texas Sw Med Ctr/Dallas Dallas, Tx 753909105

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

  Summary: Congenital heart defects are the result of abnormal development of mesodermal cells, which form the muscular portion of the heart, or neural crest-derived cells, which populate the cardiac outflow tract and aortic arches. Defects in the two population of cells usually occur in a segmental fashion resulting in abnormalities of distinct regions of the heart with neighboring regions being relatively normal. The long term goal of this proposal is to understand the independent molecular pathways and mechanisms which would control segmental cardiac development. This type of understanding is the first step in identifying the genes which cause heart defects in distinct regions of the heart. Specifically, we focus on elucidating the pathogenesis of isolated cardiac outflow tract defects and those which occur as part of DiGeorge/CATCH-22 (cardiac defects, abnormal facies, thymic hypoplasia, **cleft palate,** and hypocalcemia associated with chromosome 22 microdeletion) syndrome. In both scenarios, a high percentage of affected individuals harbor a microdeletion of one allele of chromosome 22q11.2 and are thought to have a defect in neural crest-derived cells which populate the branchial and aortic arches and cardiac outflow tract. In contrast, conditions such as hypoplasia of the right or left ventricles have been thought to be the result of flow abnormalities during cardiogenesis. Our recent targeted deletion of the basic helix- loop-helix transcription factor, dHAND, suggests that a subset of cardiac outflow tract defects and hypoplastic right ventricle may be the result of excessive programmed cell death from single gene defects. Although dHAND-null embryos have hypoplasia of the neural crest-derived branchial and aortic arches and right ventricle, dHAND does not map to human chromosome 22. However, by subtraction cloning between wild type and dHAND-null embryos, we have found that a ubiquitin fusion degradation protein (UFD1) is downstream of dHAND and maps to the DiGeorge critical region of ch.22. We have shown that UFD1 is normally expressed in the branchial arches, cardiac outflow tract and right ventricle but is down-regulated in dHAND-null embryos. The UFD family has been studied in yeast where they represent a novel proteolytic pathway for degradation of cellular proteins. Targeted deletion of UFD1 in yeast results in cell death in a dose-dependent fashion, suggesting that the down-regulation of UFD1 may mediate the apoptosis seen in dHAND mutants. Having placed UFD1 as a candidate gene for CATCH-22 syndrome from a molecular pathway and mechanistic approach, we propose three major aims for this proposal: 1) to determine, in mice, the role of UFD1 during embryogenesis and if UFD1 is one of the genes responsible for a DiGeorge/CATCH-22-like phenotype, 2) to determine if mutations and/or deletions of UFD1 in humans contribute to cardiac outflow tract defects or subsets of CATCH-22, 3) to define the role of UFD1 and dHAND in cell survival during embryonic development. The aims utilize in vivo models of yeast, mice and humans to understand the development of cardiac mesoderm and neural crest in normal and abnormal embryogenesis. In this fashion, we intend to approach the molecular basis for certain congenital heart defects, particularly those affecting the cardiac outflow tract and aortic arch in isolation and in CATCH-22 syndrome.

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

- **Project Title: TGF BETA SIGNALING AND CRANIOFACIAL MORPHOGENESIS**

  Principal Investigator & Institution: Chai, Yang; Associate Professor; Ctr/Craniofacial Molec Biol; University of Southern California 2250 Alcazar Street, Csc-219 Los Angeles, Ca 90033

  Timing: Fiscal Year 2004; Project Start 01-JAN-1999; Project End 31-MAR-2009

  Summary: (provided by applicant): **Cleft palate** represents one of the major groups of congenital birth defects in the human population. Despite recent advancements in medical intervention, babies born with **cleft palate** often suffer multiple handicaps that significantly compromise the quality of their lives. Cranial neural crest (CNC) is an important population of multipotent embryonic progenitor cells, which ultimately contribute to a diverse array of differentiated craniofacial tissues, including the palatal mesenchyme, and plays an integral role during palatogenesis. An understanding of the manner in which CNC cells contribute to palatal development and the molecular mechanism, which regulates the fate of CNC are critical for understanding normal craniofacial development as well as CNC-related congenital malformations. Multiple growth and transcription factors have been identified as critical regulators for palatogenesis. Specifically, TGF-beta plays a pivotal role in regulating the fate of medial edge epithelium during palatal fusion. It is not well understood, however, what is the functional significance of TGF-beta signaling in regulating the fate of CNC derived palatal mesenchyme. To address this issue, we have generated an animal model with conditional TGF-beta type II receptor (TGF-beta IIRfl/fl;Wnt1-Cre) gene ablation in neural crest cells. These TGF-beta IIRfl/fl;Wnt1-Cre mice show **cleft palate** and other craniofacial defects with 100 percent phenotype penetrance. Significantly, there is normal CNC migration into the first branchial arch of TGF-beta IIRfl/fl;Wnt1-Cre embryos, indicating that disruption of TGF-(signaling does not adversely affect CNC migration. Therefore, TGF-beta-mediated gene expression is specifically required locally during palatal development. Taking advantage of our TGF-beta IIRfl/fl;Wnt1-Cre and other mutant animal models we design studies to investigate the hierarchy of TGF-beta signaling in regulating the fate of CNC cells during palatogenesis by testing the hypothesis that TGF-beta signaling regulates the expression of homeobox gene Msx1, which in turn controls the progression of cell cycle to regulate the fate of CNC-derived palatal mesenchymal cells during palatogenesis. Ultimately, this study will provide a better understanding on how the TGF-beta signaling cascade regulates the fate of CNC cells during normal craniofacial development and how signaling disruption can lead to craniofacial malformations.

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

- **Project Title: TGF BETA3 IN LUNG MORPHOGENESIS, INJURY AND REPAIR**

  Principal Investigator & Institution: Groffen, John H.; Children's Hospital Los Angeles 4650 Sunset Blvd Los Angeles, Ca 90027

  Timing: Fiscal Year 2002

  Summary: Members of the transforming growth factor (TGF) family are key cytokines involved in tissue morphogenesis and repair. Todefine key functions specific to TGF-beta3, we generated TGF-beta3 null mutant mice. These shoul unique phenotypic features restricted to delayed pulmonary development and a **cleft palate** and die shortly after birth. Lungs appeared primitive with decreased alveolarization. The risk for developing neonatal lung disease. These data indicate an important role for TGF-beta in perinatal lung deelopment and we hypothesize that TGF-beta3 is involved in the pathobiology of lung disease. We propose to further determine whether the temporo-

spatial influence of TGF-beta on lung development evident from the null mutant occurs primarily during the early embryonic versus late fetalstages and whether the primary effects are on gene expression in the epithelium or mesenchyme. Candidate genes will be identified in the molecular signaling pathways through which TGF-beta3 regulates lung development and repair of lung injury, using representational difference analysis for cocmparing our TGF-beta3 null mutants and overexpressors to wild type. Effects of TGF-beta3 overexpression on lung organogenesis and repair will be investigated, as compared to the known deleterious effects of TGF-beta1, using transgenic mice overexpressing TGF-beta3 froma tightly regulatable TGF-beta3 promoter. The consequences of TGF-beta3 absence on postnatal lung development and lung repair in response to experimentally elicited pulmonary injury will be assessed in TGF-beta3 null mutants, in which the production of TGF-beta3 can be switched on and off as required. Our experiments will identify specific roles of TGF-beta3 in both lung development and repair including the development of neonatal chronic lung disease using unique in vivo mouse models. The data generated will be of importance towards the realization of the long-termgoals of this Program Project of developing rational therapeutics against neonatal pulmonary disease.

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

- **Project Title: TGFBETA SIGNALING DURING CRANIOFACIAL DEVELOPMENT**

  Principal Investigator & Institution: Greene, Robert M.; Professor; Biological & Biophysical Scis; University of Louisville University of Louisville Louisville, Ky 40292

  Timing: Fiscal Year 2002; Project Start 01-JUL-1999; Project End 30-JUN-2004

  Summary: (adapted from the Investigator's abstract): The TGF-beta family represents a class of signaling molecules that plays a central role in normal embryonic development including the developing mammalian secondary palate. Within the past few years, a family of very highly conserved proteins, Smads, which are essential components of the TGF-beta l signaling pathways, has been identified. This revised application proposes an exploration of TGF-beta/Smad cytoplasmic and nuclear signal transduction in embryonic palatal tissue. Specific studies include definition of Smads 1-8 mRNA and protein expression and distribution during palate ontogeny, an analysis of the functional role that TGF-beta/Smad signaling may play during palatal tissue differentiation, an analysis of a specific molecular mechanism by which TGF-beta induced growth inhibition may be mediated in embryonic palatal tissue and an exploration of a molecular mechanism by which TGF-beta signaling may regulate transcriptional responses. The current application proposes to test the following five hypotheses. First, Smads are expressed in distinct spatio-temporal patterns in developing palatal tissue. Second, TFG-beta induced inhibition of mesenchymal cell proliferation and/or palate medial edge epithelial differentiation is Smad mediated. Third, TGF-beta induced growth inhibition in embryonic palatal tissue is effected by a Smad-mediated up-regulation of cyclin-dependent kinase inhibitors. Fourth, Smads and the nuclear transcription factor CREB associate in a TGF-beta-stimulated DNA-binding complex to mediate transduction of the TGF-beta signal. Fifth, Smads associate with non-CREB transcription factors to form a DNA-binding complex. Craniofacial malformations occur with a frequency of 1 in 600 live births annually in the United States. This translates into the startling fact that, on average, a baby is born with a cleft in this country every hour of every day. Thus, approximately 8-9000 new cleft babies are born each year. Causes of abnormal formation of the palate are largely unknown. Hence, studies such as those proposed herein will define and clarify molecular regulatory mechanisms underlying the etiology of palatal clefts.

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

- **Project Title: THE ROLE OF TGF-BETA3 IN PALATOGENESIS**

  Principal Investigator & Institution: Kaartinen, Vesa M.; Assistant Professor; Children's Hospital Los Angeles 4650 Sunset Blvd Los Angeles, Ca 90027

  Timing: Fiscal Year 2002; Project Start 01-FEB-2001; Project End 31-DEC-2004

  Summary: The long-term goal of this proposal is to define specific molecular mechanisms of TGF-beta3-induced palatal fusion. During development TGF-beta3 expression is both spatially and temporally restricted. Exceptionally high expression levels have been found specifically in prefusion palatal epithelium. Concordant with this surge of TGF-beta3 expression, homozygous TGF-beta3-deficient mice suffer from bilateral clefting of the secondary palate. It has been suggested that during epithelial fusion, TGF-beta3 triggers epithelio-mesenchymal transdifferentiation and associated degradation of the basement membrane, processes necessary for successful palatal fusion. The combined data, including expression pattern and level of TGF-beta3 in prefusion palatal shelves, complete penetrance of **cleft palate** in TGF- beta3 null mutant mice and failure of TGF-beta3-deficient medial edge epithelial cells to transdifferentiate from epithelial cells to mesenchymal cells lead to the formulation or the following hypotheses: TGF beta3 is a master switch, capable of initiating a cascade of molecular events leading to successful midline epithelial fusion during palatogenesis. To test this hypothesis we will utilize TGF-beta3 null mutant mice to investigate TGF-beta3 signaling and downstream biological responses. The proposed studies have been organized to three different Aims: expression and function of TGF-beta type I receptors and their down- stream signaling molecules, Smads in Aim 1, role of epithelial mastergenes and key molecular switches in epithelio-mesenchymal transdifferentiation during epithelial fusion in Aim2, and function of metalloprotemases and their inhibitors during associated degradation of the basement membrane in Aim 3. These studies will eventually improve our understanding of the pathogenetic mechanisms that lead to formation of **cleft palate,** one of the most common congenital birth defects in human.

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

- **Project Title: THE ROLE OF UFD1 AND CDC45 IN NEURAL CREST DEVELOPMENT**

  Principal Investigator & Institution: Garg, Vidu; Pediatrics; University of Texas Sw Med Ctr/Dallas Dallas, Tx 753909105

  Timing: Fiscal Year 2002; Project Start 01-AUG-2000; Project End 31-JUL-2005

  Summary: (Adapted from applicant's description): The candidate's goals are to become an independent investigator and to pursue a career in academic pediatric cardiology. He will perform research under the guidance of a pediatric cardiologist with expertise in the field of cardiovascular development. While in the laboratory, he will acquire new skills in molecular biology and have access to state-of-the-art facilities. The candidate will be in a Pediatric Department that has afforded him protected research time during his fellowship. He is at a university where he will have contact with professors with extensive backgrounds in molecular and developmental biology, and that hosts lectures from eminent basic scientists from around the world. The long term objectives of the research project are to determine the role of UFD1 and CDC45 in neural crest cells during embryogenesis. Neural crest cells are involved in cardiac development, as they are important for the normal formation of the cardiac outflow tract and aortic arch arteries. The CATCH-22 (gardiac defects, abnormal facies, !hymic hypoplasia, **cleft**

palate, and itypocalcemia associated with chromosome 22 microdeletion) syndrome is believed to arise from neural crest defects. The CATCH-22 syndrome is the most common human genetic deletion with an incidence of 1/4,000 live births and is the second most common genetic cause of congenital heart disease (CHD). In CATCH-22, 90% of the patients share in common a deletion spanning 2-3 Mb of one copy of chromosome 22q II, but the gene(s) responsible have not been determined. Individuals with CATCH-22 have CHD involving the cardiac outflow tract and aortic arch arteries. UFDl and CDC45 are two of the nearly thirty genes located in the DiGeorge Critical Region (DGCR) on chromosome 22q 11. A patient with the CATCH-22 phenotype was identified who had a monoallelic deletion of the first three exons of the UFDI(ubiquitin fusion degradation protein) gene and the first five exons of a neighboring gene, CDC45 (cell-division-cycle protein). By in situ hybridization, Ufdl and Cdc45 were co-expressed in the neural crest-derived pharyngeal arches, aortic arch arteries, and cardiac outflow tract. Prior to this, HIRA, a transcriptional regulator, was the only other gene in the DGCR specifically expressed in neural crest-derived tissues during embryogenesis. The specific aims of the project are: I. To determine the function of Ufd 1 and Cdc45 in embryogenesis. 2. To determine the role of Cdc45 in neural crest development. 3. To determine if protein-protein interactions exist between Ufdl, Cdc45, and Hira. A conventional knockout strategy will be used to delete the Ufdl and Cdc45 genes in mice. Heterozygous and homozygous mice will be analyzed for neural crest defects. The function of Cdc45 will be examined in vivo in chick embryos by retrovirally mediated alteration of gene expression. A yeast two hybrid assay will be utilized to determine if Ufdl, Cdc45, and Hira interact with one another.

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

- **Project Title: TRANSCRIPTION FACTORS REGULATING PALATOGENESIS**

  Principal Investigator & Institution: Darling, Douglas S.; Mol/Cell/Craniofacial Biology; University of Louisville University of Louisville Louisville, Ky 40292

  Timing: Fiscal Year 2002; Project Start 01-MAR-2001; Project End 28-FEB-2003

  Summary: Defects in craniofacial development to **cleft palate** and/or cleft lip in more than 1 out of 1,000 births. Investigation of the molecular mechanisms of craniofacial development will lead to improved diagnosis, treatment, and prevention of these birth defects. The long term objective of this project is to understand the role of the transcription factor Zfhep in craniofacial development. Targeted disruption of the Zfhep/deltaEF-1 gene in mice created cleft secondary palate, hypertrophy of Meckel's cartilage, and perinatal death. However, it is unknown whether these facial defects are due to a direct, or indirect involvement of Zfhep in development. Defining the temporal-spacial expression of Zfhep is an essential step towards determining whether it has a direct role in craniofacial development. The specific goals of this project are to determine the expression pattern of both Zfhep-1 and Zfhep-2 in the mesenchyme and epithelium of the palate, and in Meckel's cartilage during mouse development using both in situ hybridization and immunohistochemistry. We will also investigate the expression of Zfhep during development of tooth buds. We will determine the specific cell types (pre-chrondrocytes, chrondrocytes, or hypertrophy chrondrocytes) expressing Zfhep during development of Meckel's cartilage. The results of this R03 application will provide a complete picture of the temporal and spatial expression pattern of Zfhep during craniofacial development, and demonstrate where Zfhep can have direct effects on development. Subsequent work will investigate the molecular mechanism(s) of Zfhep action during craniofacial development.

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

- **Project Title: VELOCARDIOFACIAL SYNDROME-MOLECULAR AND CLINICAL STUDIES**

  Principal Investigator & Institution: Emanuel, Beverly S.; Professor; Children's Hospital of Philadelphia 34Th St and Civic Ctr Blvd Philadelphia, Pa 19104

  Timing: Fiscal Year 2002; Project Start 01-APR-1994; Project End 31-JAN-2004

  Summary: Velocardiofacial syndrome (VCFS) is one of several disorders caused by a deletion of 22q11.2. It occurs with a frequency of 1/4000 livebirths and the deletion endpoints appear to cluster. VCFS patients have a spectrum of abnormalities including: **cleft palate,** speech language and learning disabilities, a typical facial appearance and cardiac defects. The frequency of the 22q11.2 deletion and complexity of the phenotype makes VCFS a significant health problem in the population. Understanding the pathogenesis of this disorder will require characterization of the deleted genes and investigations into the role that these genes play in normal embryonic and postnatal development. Thus, we will analyze the function, cell biology and expression of the genes in the deleted region as well as perform mutational analysis of the of "candidate" genes in non- deleted VCFS patients (Project 1). By chromosome engineering we will create and carefully characterize mouse models of VCFS, creating haploinsufficiency for the gens that have been identified to assess their role in the etiology of the phenotype (Project 2). The cytogenetic mechanism(s) responsible for the frequent 22q11.2 deletions will be examined by isolating and analyzing the recurrent deletion endpoints, searching for atypical deletions, studying 22q11.2 organization and analysis of chromosomal segregation/recombination (Project 3). Finally, we will seem to identify factors that influence the palatal phenotype in order to determine the source(s) of phenotypic variability seen in the deleted population (Project 4). The studies will be supported by three technical cores: A) a Clinical Core to perform detailed genetic, physical and neuropsychological examinations on the patients and manage/analyze the patient data; B) a Cell Culture Core to establish a bank of patient cell lines and DNAs; and C) a Histology core to assist in gene characterization. Capitalizing on extensive preliminary data generated by this consortium of collaborators we will continue or clinical and laboratory-based investigation of VCFS. The latest technologies in molecular genetics, mouse genetics, clinical genetics, developmental biology and physical diagnosis will be applied to dissection of this syndrome. This renewal represents a team effort aimed at detailed molecular characterization of the region of 22q11.2 deleted in VCFS to ascertain and analyze the factors responsible for creating the deletion and the complex phenotype it produces.

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

- **Project Title: VELOPHARYNGEAL FUNCTION FOR SPEECH AFTER PALATAL SURGERY**

  Principal Investigator & Institution: Williams, William N.; Director and Professor; Oral Biology; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2002; Project Start 30-SEP-1994; Project End 30-JUN-2005

  Summary: The incidence of cleft lip/palate is 1/750, making it one of the most common congenital malformations. The primary goal in surgically repairing the palatal cleft is to construct a competent velopharyngeal port for the development of normal speech. Failure to establish velopharyngeal competency results in speech characterized by hypernasality, loss of intraoral air pressure through the nose, and articulation disorders. The University of Florida, in collaboration with the University of Sao Paulo, Bauru, Brazil, is proposing a five-year continuation prospective randomized, controlled study

to complete the assessment of velopharyngeal function for speech following palatoplasty (by the von Langenbeck procedure with intravelar velar plasty, and the Furlow double opposing z-plasty palatoplasty) for 352 subjects with complete unilateral cleft lip and palate. The von Langenbeck procedure has been selected as the time tested standard against which the Furlow procedure can be judged. The Furlow procedure has been reported to yield higher rates of velopharyngeal competency than identified in most other reported series, which also theoretically should result in less disturbance to mid-facial growth. Fewer patients than projected (explained in the text), were available for enrollment by the end of the initial study (9/99), and less than 50 were old enough for reliable assessment of their velopharyngeal competency for speech. Continuation of the study will allow enrollment of all 352 patients and the comparison of results between patients operated between 9-12 months of age and patients 15-18 months of age. Perceptual and instrumental measures of speech and velopharyngeal function will be obtained on all patients within the five year time frame of the proposed project. Facial growth analysis, although not a part of the proposed study, will continue until all patients reach maturity. The clinical caseload at the University of Sao Paulo currently exceeds 29,000 and over 1,500 new cases of cleft lip/palate are added yearly. This project represents a unique opportunity to obtain prospective data with a large number of subjects, controlling the variables which have traditionally plagued **cleft palate** studies. This study should definitively answer the question of which of the two surgical procedures is superior in constructing a velum capable of effecting velopharyngeal competency for the development of normal speech. In addition, this study may serve as a model for international prospective clinical trials, such as in Russia and Ukraine where treatment of **cleft palate** is centralized.

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 "cleft palate" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for cleft palate in the PubMed Central database:

- **Cleft palate and decreased brain [gamma]-aminobutyric acid in mice lacking the 67-kDa isoform of glutamic acid decarboxylase.** by Asada H, Kawamura Y, Maruyama K, Kume H, Ding RG, Kanbara N, Kuzume H, Sanbo M, Yagi T, Obata K.; 1997 Jun 10; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=21078

[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.

- **Cleft palate in mice with a targeted mutation in the [gamma]-aminobutyric acid-producing enzyme glutamic acid decarboxylase 67.** by Condie BG, Bain G, Gottlieb DI, Capecchi MR.; 1997 Oct 14;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=23502
- **Concordance Between Isolated Cleft Palate in Mice and Alterations Within a Region Including the Gene Encoding the [beta]3 Subunit of the Type A [gamma]-Aminobutyric Acid Receptor.** by Culiat CT, Stubbs L, Nicholls RD, Montgomery CS, Russell LB, Johnson DK, Rinchik EM.; 1993 Jun 1;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=46663
- **Craniofacial Dysmorphogenesis Including Cleft Palate in Mice with an Insertional Mutation in the discs large Gene.** by Caruana G, Bernstein A.; 2001 Mar 1;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=86693
- **Genome scan for teratogen-induced clefting susceptibility loci in the mouse: Evidence of both allelic and locus heterogeneity distinguishing cleft lip and cleft palate.** by Diehl SR, Erickson RP.; 1997 May 13;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=24661
- **Isolated cleft palate in mice with a targeted mutation of the LIM homeobox gene Lhx8.** by Zhao Y, Guo YJ, Tomac AC, Taylor NR, Grinberg A, Lee EJ, Huang S, Westphal H.; 1999 Dec 21;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=24762
- **Mice devoid of [gamma]-aminobutyrate type A receptor [beta]3 subunit have epilepsy, cleft palate, and hypersensitive behavior.** by Homanics GE, DeLorey TM, Firestone LL, Quinlan JJ, Handforth A, Harrison NL, Krasowski MD, Rick CE, Korpi ER, Makela R, Brilliant MH, Hagiwara N, Ferguson C, Snyder K, Olsen RW.; 1997 Apr 15;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=20582

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 cleft palate, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "cleft palate" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for cleft palate (hyperlinks lead to article summaries):

[6] PubMed was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The PubMed database was developed in conjunction with publishers of biomedical literature as a search tool for accessing literature citations and linking to full-text journal articles at Web sites of participating publishers. Publishers that participate in PubMed supply NLM with their citations electronically prior to or at the time of publication.

- **A bilateral musculomucosal buccal flap method for cleft palate surgery.**
  Author(s): Chen GF, Zhong LP.
  Source: Journal of Oral and Maxillofacial Surgery : Official Journal of the American Association of Oral and Maxillofacial Surgeons. 2003 December; 61(12): 1399-404.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14663803&dopt=Abstract
- **A family with distal arthrogryposis and cleft palate: possible overlap between Gordon syndrome and Aase-Smith syndrome.**
  Author(s): Becker K, Splitt M.
  Source: Clinical Dysmorphology. 2001 January; 10(1): 41-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11152147&dopt=Abstract

- **A feeding adaptation by an infant with a cleft palate.**
  Author(s): Sykes L, Essop R.
  Source: Sadj. 1999 August; 54(8): 369-70.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10860048&dopt=Abstract

- **A method of "unilateral operation" for early repair of unilateral complete cleft palate. Preliminary report.**
  Author(s): Song R, Song Y, Liu C, Ma H, Zhao Y, Zhao R, Fang Z.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 2000 May; 37(3): 243-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10830802&dopt=Abstract

- **A novel loss-of-function mutation in TTF-2 is associated with congenital hypothyroidism, thyroid agenesis and cleft palate.**
  Author(s): Castanet M, Park SM, Smith A, Bost M, Leger J, Lyonnet S, Pelet A, Czernichow P, Chatterjee K, Polak M.
  Source: Human Molecular Genetics. 2002 August 15; 11(17): 2051-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12165566&dopt=Abstract

- **A pilot study of the effects of transpalatal maxillary advancement on velopharyngeal closure in cleft palate patients.**
  Author(s): Sell D, Ma L, James D, Mars M, Sheriff M.
  Source: Journal of Cranio-Maxillo-Facial Surgery : Official Publication of the European Association for Cranio-Maxillo-Facial Surgery. 2002 December; 30(6): 349-54.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12425989&dopt=Abstract

- **A retrospective study of speech development in patients with submucous cleft palate treated by four operations.**
  Author(s): Park S, Saso Y, Ito O, Tokioka K, Kato K, Nitta N, Kitano I.
  Source: Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery / Nordisk Plastikkirurgisk Forening [and] Nordisk Klubb for Handkirurgi. 2000 June; 34(2): 131-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10900628&dopt=Abstract

- **A six-centre international study of the outcome of treatment in patients with clefts of the lip and palate: the results of a cross-linguistic investigation of cleft palate speech.**
  Author(s): Grunwell P, Brondsted K, Henningsson G, Jansonius K, Karling J, Meijer M, Ording U, Wyatt R, Vermeij-Zieverink E, Sell D.
  Source: Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery / Nordisk Plastikkirurgisk Forening [and] Nordisk Klubb for Handkirurgi. 2000 September; 34(3): 219-29.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11020918&dopt=Abstract

- **A technique for cleft palate repair.**
  Author(s): Sommerlad BC.
  Source: Plastic and Reconstructive Surgery. 2003 November; 112(6): 1542-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14578783&dopt=Abstract

- **Abnormal brain morphology in patients with isolated cleft lip, cleft palate, or both: a preliminary analysis.**
  Author(s): Nopoulos P, Berg S, Canady J, Richman L, Van Demark D, Andreasen NC.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 2000 September; 37(5): 441-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11034025&dopt=Abstract

- **Active participation of mothers during speech therapy improved language development of children with cleft palate.**
  Author(s): Pamplona MC, Ysunza A.
  Source: Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery / Nordisk Plastikkirurgisk Forening [and] Nordisk Klubb for Handkirurgi. 2000 September; 34(3): 231-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11020919&dopt=Abstract

- **Adult skeletal profile in isolated cleft palate: a comparison of the von Langenbeck and Wardill procedures for primary repair of the palate.**
  Author(s): Becker M, Svensson H, McWilliam J, Sarnas KV, Jacobsson S.
  Source: Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery / Nordisk Plastikkirurgisk Forening [and] Nordisk Klubb for Handkirurgi. 2001 December; 35(4): 387-97.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11878175&dopt=Abstract

- **Aerodynamic and cephalometric analyses of velopharyngeal structure and function following re-pushback surgery for secondary correction in cleft palate.**
  Author(s): Nakamura N, Ogata Y, Sasaguri M, Suzuki A, Kikuta R, Ohishi M.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 2003 January; 40(1): 46-53.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12498605&dopt=Abstract

- **Aesthetic dilemma: restoring the quality of life in a cleft lip, cleft palate patient.**
  Author(s): Mopper KW.
  Source: Dent Today. 2000 June; 19(6): 46-8, 50-3. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12524792&dopt=Abstract

- **An electropalatographic investigation of middorsum palatal stops in an adult with repaired cleft palate.**
  Author(s): Gibbon FE, Crampin L.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 2001 March; 38(2): 96-105.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11294548&dopt=Abstract

- **An international surgical exchange program for children with cleft lip/cleft palate in Manaus, Brazil: patient and family expectations of outcome.**
  Author(s): Reeve ME, Groce NE, Persing JA, Magge SN.
  Source: The Journal of Craniofacial Surgery. 2004 January; 15(1): 170-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14704585&dopt=Abstract

- **An osteotome for outfracture of the greater palatine foramen in cleft palate repair.**
  Author(s): Oh A, Wong GB.
  Source: Plastic and Reconstructive Surgery. 2001 March; 107(3): 820-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11304611&dopt=Abstract

- **Articulation disorders associated with maxillary growth after attainment of normal articulation after primary palatoplasty for cleft palate.**
  Author(s): Oyama T, Sunakawa H, Arakaki K, Shinya T, Tengan T, Hiratsuka H, Maekawa T.
  Source: Annals of Plastic Surgery. 2002 February; 48(2): 138-47.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11910218&dopt=Abstract

- **Assessing intelligibility in speakers with cleft palate: a critical review of the literature.**
  Author(s): Whitehill TL.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 2002 January; 39(1): 50-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11772170&dopt=Abstract

- **Association of cleft palate with Sprengel anomaly: confirmation of the Hodgson-Chiu syndrome.**
  Author(s): Monier A, Van Maldergem L, Stevens R.
  Source: American Journal of Medical Genetics. 2000 December 11; 95(4): 401-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11186899&dopt=Abstract

- **Bent JP 3rd, Klippert FN, Smith RJH. Management of congenital buccopharyngeal membrane. Cleft Palate Craniofac J 1997;34:538-541.**
  Author(s): Agarwal R, Chandra R.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 1999 March; 36(2): 179-80.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10213065&dopt=Abstract

- **Bifid tongue associated with midline cleft palate, mandible, cervical vertebrae and linea alba.**
  Author(s): Lu CY, Teng RJ, Hou JW, Cheng TJ.
  Source: European Journal of Pediatrics. 1998 January; 157(1): 86.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9461373&dopt=Abstract

- **Bilateral microtia and cleft palate in cousins with Diamond-Blackfan anemia.**
  Author(s): Gripp KW, McDonald-McGinn DM, La Rossa D, McGain D, Federman N, Vlachos A, Glader BE, McKenzie SE, Lipton JM, Zackai EH.
  Source: American Journal of Medical Genetics. 2001 July 1; 101(3): 268-74.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11424144&dopt=Abstract

- **Biologic basis for a risk assessment model for cleft palate.**
  Author(s): Freni SC, Zapisek WF.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 1991 October; 28(4): 338-46. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1742301&dopt=Abstract

- **Birth weight and gestational age of newborns with cleft lip with or without cleft palate and with isolated cleft palate.**
  Author(s): Wyszynski DF, Sarkozi A, Vargha P, Czeizel AE.
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  Author(s): Braybrook C, Doudney K, Marcano AC, Arnason A, Bjornsson A, Patton MA, Goodfellow PJ, Moore GE, Stanier P.
  Source: Nature Genetics. 2001 October; 29(2): 179-83.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11559848&dopt=Abstract

- **The use of the operating microscope for cleft palate repair and pharyngoplasty.**
  Author(s): Sommerlad BC.
  Source: Plastic and Reconstructive Surgery. 2003 November; 112(6): 1540-1.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14578782&dopt=Abstract

- **Three-dimensional morphology of the palate in subjects with isolated cleft palate at the stage of permanent dentition.**
  Author(s): Smahel Z, Trefny P, Formanek P, Mullerova Z, Peterka M.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 2003 November; 40(6): 577-84.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14577820&dopt=Abstract

- **Toward pathogenesis of Apert cleft palate: FGF, FGFR, and TGF beta genes are differentially expressed in sequential stages of human palatal shelf fusion.**
  Author(s): Britto JA, Evans RD, Hayward RD, Jones BM.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 2002 May; 39(3): 332-40.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12019011&dopt=Abstract

- **Tympanoplasty results in patients with cleft palate: an age- and procedure-matched comparison of preliminary results with patients without cleft palate.**
  Author(s): Gardner E, Dornhoffer JL.
  Source: Otolaryngology and Head and Neck Surgery. 2002 May; 126(5): 518-23.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12075226&dopt=Abstract

- **Uncommon Klinefelter's variant (49,XXXXY) with cleft palate.**
  Author(s): Velidedeoglu HV, Demir Z, Bozdogan MN, Coskunfirat OK, Kurtay A, Turkguven Y.
  Source: Annals of Plastic Surgery. 1997 August; 39(2): 213-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9262781&dopt=Abstract

- **Unilateral cleft lip with or without cleft palate and handedness: is there an association?**
  Author(s): Daskalogiannakis J, Kuntz KL, Chudley AE, Ross RB.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 1998 January; 35(1): 46-51.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9482223&dopt=Abstract

- **Unusual presentation of gastroesophageal reflux with corpus callosum agenesis, cleft palate and mental retardation.**
  Author(s): Desai BN, Joshi SM, Malik S, Mittal S, Dandge VP.
  Source: Indian Pediatrics. 1991 November; 28(11): 1328-30.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1808058&dopt=Abstract

- **Use of a consensus building approach to plan speech services for children with cleft palate in India.**
  Author(s): D'Antonio LL, Nagarajan R.
  Source: Folia Phoniatrica Et Logopaedica : Official Organ of the International Association of Logopedics and Phoniatrics (Ialp). 2003 November-December; 55(6): 306-13.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14573987&dopt=Abstract

- **Use of cartilage grafts for closure of cleft palate fistulae.**
  Author(s): Jeffery SL, Boorman JG, Dive DC.
  Source: British Journal of Plastic Surgery. 2000 October; 53(7): 551-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11000068&dopt=Abstract

- **Use of distraction osteogenesis in cleft palate patients.**
  Author(s): Tae KC, Gong SG, Min SK, Oh SW.
  Source: Angle Orthod. 2003 October; 73(5): 602-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14580030&dopt=Abstract

- **Use of hearing aids in the management of children with cleft palate.**
  Author(s): Maheshwar AA, Milling MA, Kumar M, Clayton MI, Thomas A.
  Source: International Journal of Pediatric Otorhinolaryngology. 2002 October 21; 66(1): 55-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12363423&dopt=Abstract

- **Use of the Arndt nickel titanium palatal expander in cleft palate cases.**
  Author(s): Abdoney MO.
  Source: J Clin Orthod. 1995 August; 29(8): 496-9. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9063155&dopt=Abstract

- **Use of the Branemark implant in the cleft palate patient.**
  Author(s): Verdi FJ Jr, SLanzi GL, Cohen SR, Powell R.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 1991 July; 28(3): 301-3; Discussion 304.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1911819&dopt=Abstract

- **Uvular transposition: a new method of cleft palate repair.**
  Author(s): David LR, Blalock D, Argenta LC.
  Source: Plastic and Reconstructive Surgery. 1999 September; 104(4): 897-904.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10654725&dopt=Abstract

- **Variable expression of rib, pectus, and scapular anomalies with Robin-type cleft palate in a 5-generation family: a new syndrome?**
  Author(s): Stalker HJ, Zori RT.
  Source: American Journal of Medical Genetics. 1997 December 19; 73(3): 247-50.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9415678&dopt=Abstract

- **Velopharyngeal (speech) disorder (VP(S)D) without overt cleft palate.**
  Author(s): Pigott RW.
  Source: British Journal of Plastic Surgery. 1994 June; 47(4): 223-9. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8081608&dopt=Abstract

- **Velopharyngeal assessment procedures for the Thai cleft palate population.**
  Author(s): Garrett JD, Deal RE, Prathanee B.
  Source: J Med Assoc Thai. 2002 June; 85(6): 682-92.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12322841&dopt=Abstract

- **Velopharyngeal function from the age of three to eight years in cleft palate patients.**
  Author(s): Pulkkinen J, Haapanen ML, Paaso M, Laitinen J, Ranta R.
  Source: Folia Phoniatrica Et Logopaedica : Official Organ of the International Association of Logopedics and Phoniatrics (Ialp). 2001 March-April; 53(2): 93-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11244283&dopt=Abstract

- **Velopharyngeal function in nonsyndromic cleft palate: relevance of surgical technique, age at repair, and cleft type.**
  Author(s): Marrinan EM, LaBrie RA, Mulliken JB.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 1998 March; 35(2): 95-100. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9527305&dopt=Abstract

- **Velopharyngeal morphology of patients with persistent velopharyngeal incompetence following repushback surgery for cleft palate.**
  Author(s): Nakamura N, Ogata Y, Kunimitsu K, Suzuki A, Sasaguri M, Ohishi M.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 2003 November; 40(6): 612-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14577815&dopt=Abstract

- **Videonasopharyngoscopy as an instrument for visual biofeedback during speech in cleft palate patients.**
  Author(s): Ysunza A, Pamplona M, Femat T, Mayer I, Garcia-Velasco M.
  Source: International Journal of Pediatric Otorhinolaryngology. 1997 September 18; 41(3): 291-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9350488&dopt=Abstract

- **Vocal development of 9-month-old babies with cleft palate.**
  Author(s): Chapman KL, Hardin-Jones M, Schulte J, Halter KA.
  Source: Journal of Speech, Language, and Hearing Research : Jslhr. 2001 December; 44(6): 1268-83.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11776364&dopt=Abstract

- **Voluntary health care for children with unrepaired cleft lip and cleft palate in developing countries--a personal perspective.**
  Author(s): McGovern E.
  Source: J Ir Dent Assoc. 2003; 49(4): 142-4. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14705365&dopt=Abstract

- **Von Langenbeck or Wardill procedures for primary palatal repair in patients with isolated cleft palate--speech results.**
  Author(s): Becker M, Svensson H, Sarnas KV, Jacobsson S.
  Source: Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery / Nordisk Plastikkirurgisk Forening [and] Nordisk Klubb for Handkirurgi. 2000 March; 34(1): 27-32.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10756573&dopt=Abstract

- **Webbing of the pharyngeal recess in adults with cleft palate.**
  Author(s): Walter JD.
  Source: Cleft Palate J. 1990 October; 27(4): 411-3; Discussion 414. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2253389&dopt=Abstract

- **What syndrome is this? Ectrodactyly, ectodermal dysplasia, and cleft palate (EEC) syndrome.**
  Author(s): Miller CI, Hashimoto K, Shwayder T, el-Hoshy K, Horton S.
  Source: Pediatric Dermatology. 1997 May-June; 14(3): 239-40.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9192423&dopt=Abstract

- **Wide cleft palate repaired by brachial flap.**
  Author(s): Namin AH.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 1992 March; 29(2): 192-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1571355&dopt=Abstract

CHAPTER 2. NUTRITION AND CLEFT PALATE

Overview

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

Finding Nutrition Studies on Cleft Palate

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 "cleft palate" (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 "cleft palate" (or a synonym):

- **A one-visit obturator technique for infants with cleft palate.**
  Author(s): Department of Restorative Dentistry, University of Medicine and Dentistry, New Jersey Dental School, Newark 07103.
  Source: Samant, A J-Oral-Maxillofac-Surg. 1989 May; 47(5): 539-40 0278-2391

- **A report on the hazards encountered when taking neonatal cleft palate impressions (1983-1992).**
  Author(s): Orthodontic Department, Essex County Hospital, Colchester.
  Source: Chate, R A Br-J-Orthod. 1995 November; 22(4): 299-307 0301-228X

- **Alteration in the expression of bone morphogenetic protein-2,3,4,5 mRNA during pathogenesis of cleft palate in BALB/c mice.**
  Author(s): Department of Oral Pathology, Stomatological College, Xi'an, People's Republic of China.
  Source: Lu, H Jin, Y Tipoe, G L Arch-Oral-Biol. 2000 February; 45(2): 133-40 0003-9969

- **Alteration of apoptosis in cleft palate formation and ectomesenchymal stem cells influenced by retinoic acid.**
  Author(s): Department of Oral Histology and Pathology, Stomatological College, Fourth Military Medical University, Xi'an, P.R. China.
  Source: Suwa, F Jin, Y Lu, H Li, X Tipoe, G L Lau, T Y Tamada, Y Kuroki, K Fang, Y R Okajimas-Folia-Anat-Jpn. 2001 December; 78(5): 179-86 0030-154X

- **An in vitro screening system for characterizing the cleft palate-inducing potential of chemicals and underlying mechanisms.**
  Author(s): Toxicology Division I, Institute of Environmental Toxicology, 4321 Uchimoriya-machi, Mitsukaido-shi, 303-0043, Ibaraki, Japan
  Source: Shimizu, N Aoyama, H Hatakenaka, N Kaneda, M Teramoto, S Reprod-Toxicol. 2001 November; 15(6): 665-72 0890-6238

- **B group vitamins and cleft lip and cleft palate.**
  Author(s): Universitatsklinik fur Mund, -Kiefer- und Plastische Gesichtschirurgie, Martin-Luther-Universitat Halle-Wittenberg, Germany.
  Source: Schubert, J Schmidt, R Syska, E Int-J-Oral-Maxillofac-Surg. 2002 August; 31(4): 410-3 0901-5027

- **Comparison of cleft palate induction by Nicotiana glauca in goats and sheep.**
  Author(s): United States Department of Agriculture, Agricultural Research Service, Poisonous Plant Research Laboratory, Logan, Utah 84341, USA. kpanter@cc.usu.edu
  Source: Panter, K E Weinzweig, J Gardner, D R Stegelmeier, B L James, L F Teratology. 2000 March; 61(3): 203-10 0040-3709

- **Diphenylhydantoin affects glycosaminoglycans and collagen production by human fibroblasts from cleft palate patients.**
  Author(s): Istituto di Istologia ed Embriologia Generale, Universita degli Studi di Ferrara, Italy.
  Source: Bosi, G Evangelisti, R Valeno, V Carinci, F Pezzetti, F Calastrini, C Bodo, M Carinci, P J-Dent-Res. 1998 August; 77(8): 1613-21 0022-0345

- **Lack of evidence for a significant association between nonsyndromic cleft lip with or without cleft palate and the retinoic acid receptor alpha gene in the Japanese population.**
  Author(s): Department of Plastic Surgery, Tohoku University School of Medicine, Sendai, Japan.

Source: Kanno, K Suzuki, Y Yang, X Yamada, A Aoki, Y Kure, S Matsubara, Y J-Hum-Genet. 2002; 47(6): 269-74 1434-5161

- **Linkage disequilibrium between GABRB3 gene and nonsyndromic familial cleft lip with or without cleft palate.**
  Author(s): Department of Morphology and Embryology, Section of Histology and Embryology, University of Ferrara, Via Fossato di Mortara 64/B, 44100 Ferrara, Italy.
  Source: Scapoli, Luca Martinelli, Marcella Pezzetti, Furio Carinci, Francesco Bodo, Maria Tognon, Mauro Carinci, Paolo Hum-Genet. 2002 January; 110(1): 15-20 0340-6717

- **Mesenchymal changes associated with retinoic acid induced cleft palate in CD-1 mice.**
  Author(s): Department of Veterinary Biosciences, University of Illinois at Urbana-Champaign 61801, USA.
  Source: Degitz, S J Francis, B M Foley, G L J-Craniofac-Genet-Dev-Biol. 1998 Apr-June; 18(2): 88-99 0270-4145

- **Pathogenesis of cleft palate in Treacher Collins, Nager, and Miller syndromes.**
  Author(s): Department of Cell Biology and Anatomy, University of North Carolina, Chapel Hill 27599.
  Source: Sulik, K K Smiley, S J Turvey, T A Speight, H S Johnston, M C Cleft-Palate-J. 1989 July; 26(3): 209-16; discussion 216 0009-8701

- **Phenytoin-induced cleft palate: evidence for embryonic cardiac bradyarrhythmia due to inhibition of delayed rectifier K+ channels resulting in hypoxia-reoxygenation damage.**
  Author(s): Department of Pharmaceutical Biosciences, Division of Toxicology, Uppsala University, S-751 24 Uppsala, Sweden.
  Source: Azarbayjani, F Danielsson, B R Teratology. 2001 March; 63(3): 152-60 0040-3709

- **Preoperative and postoperative nutritional management of the infant with cleft palate.**
  Source: Wellman, C O Coughlin, S M J-Pediatr-Nurs. 1991 June; 6(3): 154-8 0882-5963

- **Role of TGF-beta in RA-induced cleft palate in CD-1 mice.**
  Author(s): Department of Veterinary Biosciences, University of Illinois at Urbana-Champaign 61801, USA.
  Source: Degitz, S J Morris, D Foley, G L Francis, B M Teratology. 1998 November; 58(5): 197-204 0040-3709

- **The role of RXR-alpha in retinoic acid-induced cleft palate as assessed with the RXR-alpha knockout mouse.**
  Author(s): Department of Molecular, Cellular and Craniofacial Biology, University of Louisville School of Dentistry and University of Louisville Birth Defects Center, KY 40292, USA. pfnuge01@gwise.louisville.edu
  Source: Nugent, P Sucov, H M Pisano, M M Greene, R M Int-J-Dev-Biol. 1999 September; 43(6): 567-70 0214-6282

- **Vitamin A-enhanced cleft palate susceptibility associated with H-2.**
  Author(s): Medical Service, Wadsworth VA Medical Center, Los Angeles, CA 90073.
  Source: Tyan, M L J-Immunogenet. 1987 Aug-October; 14(4-5): 239-45 0305-1811

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 cleft palate; 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:

- **Vitamins**

  Folic Acid
  Source: Healthnotes, Inc.; www.healthnotes.com

CHAPTER 3. ALTERNATIVE MEDICINE AND CLEFT PALATE

Overview

In this chapter, we will begin by introducing you to official information sources on complementary and alternative medicine (CAM) relating to cleft palate. 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 cleft palate 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 "cleft palate" (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 cleft palate:

- **A short history of the treatment of cleft lip and cleft palate.**
  Author(s): Goldberg HJ, Pinsky TM, Jones NE.
  Source: Bull Hist Dent. 1977 October; 25(2): 71-8. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=346100&dopt=Abstract

- **An inquiry into the minimal amount of auditory deprivation which results in a cognitive effect in man.**
  Author(s): Ruben RJ.
  Source: Acta Otolaryngol Suppl. 1984; 414: 157-64. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6398606&dopt=Abstract

- **Asian-American cultural perspectives on birth defects: focus on cleft palate.**
  Author(s): Cheng LR.

Source: Cleft Palate J. 1990 July; 27(3): 294-300. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2197040&dopt=Abstract

- **Assessment of the protective activity of monisoamyl meso-2,3-dimercaptosuccinate against methylmercury-induced maternal and embryo/fetal toxicity in mice.**
  Author(s): Belles M, Sanchez DJ, Gomez M, Domingo JL, Jones MM, Singh PK.
  Source: Toxicology. 1996 January 8; 106(1-3): 93-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8571406&dopt=Abstract

- **Attempts to modify the frequency of cortisone-induced cleft palate in mice by vitamin, carbohydrate, and protein supplementation.**
  Author(s): KALTER H.
  Source: Plastic and Reconstructive Surgery. 1959 November; 24: 498-504.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14404192&dopt=Abstract

- **B group vitamins and cleft lip and cleft palate.**
  Author(s): Schubert J, Schmidt R, Syska E.
  Source: International Journal of Oral and Maxillofacial Surgery. 2002 August; 31(4): 410-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12361075&dopt=Abstract

- **Beyond Pierre Robin sequence.**
  Author(s): Prows CA, Bender PL.
  Source: Neonatal Netw. 1999 August; 18(5): 13-9. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10693474&dopt=Abstract

- **Brain dysfunction in neonates with cleft palate revealed by the mismatch negativity.**
  Author(s): Cheour M, Ceponiene R, Hukki J, Haapanen ML, Naatanen R, Alho K.
  Source: Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology. 1999 February; 110(2): 324-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10210622&dopt=Abstract

- **Case-control study of periconceptional folic acid supplementation and oral clefts.**
  Author(s): Hayes C, Werler MM, Willett WC, Mitchell AA.
  Source: American Journal of Epidemiology. 1996 June 15; 143(12): 1229-34.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8651221&dopt=Abstract

- **Cleft palate rehabilitation: interim strategies in Indonesia.**
  Author(s): Willcox DS.

Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 1994 July; 31(4): 316-20.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7918528&dopt=Abstract

- **Combined cleft and craniofacial team--multidisciplinary approach to cleft management.**
  Author(s): Chen YR, Chen SH, Wang CY, Noordhoff MS.
  Source: Ann Acad Med Singapore. 1988 July; 17(3): 339-42.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3218923&dopt=Abstract

- **Comparative anti-caries effects of tablet and liquid fluorides in cleft children.**
  Author(s): Lin YT, Tsai CL.
  Source: J Clin Dent. 2000; 11(4): 104-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11460274&dopt=Abstract

- **Cortical auditory dysfunction in children with oral clefts: relation with cleft type.**
  Author(s): Ceponiene R, Hukki J, Cheour M, Haapanen ML, Ranta R, Naatanen R.
  Source: Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology. 1999 November; 110(11): 1921-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10576488&dopt=Abstract

- **Cultural "iatrogenic" cleft palate.**
  Author(s): Barakat AY, Itani U, Zaytoun GM.
  Source: Pediatrics. 1986 September; 78(3): 511.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3748690&dopt=Abstract

- **Electropalatography treatment in an adult with late repair of cleft palate.**
  Author(s): Whitehill TL, Stokes SF, Yonnie MY.
  Source: The Cleft Palate-Craniofacial Journal : Official Publication of the American Cleft Palate-Craniofacial Association. 1996 March; 33(2): 160-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8695625&dopt=Abstract

- **Evidence in infants with cleft palate that breast milk protects against otitis media.**
  Author(s): Paradise JL, Elster BA, Tan L.
  Source: Pediatrics. 1994 December; 94(6 Pt 1): 853-60.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7971001&dopt=Abstract

- **First results of early speech readiness program in cleft palate children.**
  Author(s): Bickel J.
  Source: Cleft Palate J. 1970 January; 7: 156-60. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5266328&dopt=Abstract

- **Play therapy for children with cleft palates.**
  Author(s): Irwin EC, McWilliams BJ.
  Source: Children Today. 1974 May-June; 3(3): 18-22.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4464044&dopt=Abstract

- **Sex-related differences in procarbazine-induced cleft palate and microgenia and the anti-teratogenic effect of prenatal folic acid supplementation in rats.**
  Author(s): Malek FA, Moritz KU, Fanghanel J, Bienengraber V.
  Source: Ann Anat. 2003 October; 185(5): 465-70.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14575274&dopt=Abstract

- **Some implications of superstitions and folk beliefs for counseling parents of children with cleft lip and cleft palate.**
  Author(s): Crocker EC, Crocker C.
  Source: Cleft Palate J. 1970 January; 7: 124-8. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5266325&dopt=Abstract

- **Studies on a site-specific cleft palate teratogen. The toxic extract from Indigofera spicata Forssk.**
  Author(s): Pearn JH.
  Source: Br J Exp Pathol. 1967 December; 48(6): 620-6. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6079980&dopt=Abstract

- **Surgical correction of submucous cleft palate with Furlow palatoplasty.**
  Author(s): Chen PK, Wu J, Hung KF, Chen YR, Noordhoff MS.
  Source: Plastic and Reconstructive Surgery. 1996 May; 97(6): 1136-46; Discussion 1147-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8628796&dopt=Abstract

- **The Cleft Palate and Lip Society.**
  Author(s): Bodhander B.
  Source: Australas Nurses J. 1980 October; 9(11): 25. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6905752&dopt=Abstract

- **Videonasopharyngoscopy as an instrument for visual biofeedback during speech in cleft palate patients.**
  Author(s): Ysunza A, Pamplona M, Femat T, Mayer I, Garcia-Velasco M.
  Source: International Journal of Pediatric Otorhinolaryngology. 1997 September 18; 41(3): 291-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9350488&dopt=Abstract

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 cleft palate; 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**

  Birth Defects Prevention
  Source: Healthnotes, Inc.; www.healthnotes.com

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 CLEFT PALATE

Overview

In this chapter, we will give you a bibliography on recent dissertations relating to cleft palate. 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 "cleft palate" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on cleft palate, we have not necessarily excluded non-medical dissertations in this bibliography.

Dissertations on Cleft Palate

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 cleft palate. 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:

- **A Descriptive Study of the Speech Development of a Group of Infants with Unoperated Cleft Palate** by Olson, Don Andrew, PhD from Northwestern University, 1965, 203 pages
  http://wwwlib.umi.com/dissertations/fullcit/6602736
- **A Histological and Molecular Analysis of Levator Veli Palatini in a Population of Subjects with Cleft Palate** by Collins, Dana Rose, PhD from The University of Iowa, 2003, 155 pages
  http://wwwlib.umi.com/dissertations/fullcit/3087616
- **A Study of Knowledge and Concerns of Parents of Cleft Palate Children** by Cantu, Evangelina, PhD from The University of Texas at Austin, 1991, 247 pages
  http://wwwlib.umi.com/dissertations/fullcit/9212497
- **Behavior and Achievement of Cleft Palate Children** by Richman, Lynn Charles, PhD from The University of Iowa, 1973, 89 pages
  http://wwwlib.umi.com/dissertations/fullcit/7330977

- **Dermatoglyphic Variability and Asymmetry of Patients with Cleft Lip and Cleft Palate.** by Owsley, Douglas William, PhD from The University of Tennessee, 1978, 195 pages
  http://wwwlib.umi.com/dissertations/fullcit/7911701
- **Genetics and Epigenetics of Cortisone-Induced Cleft Palate in the Mouse** by Vekemans, M. J. J.; PhD from McGill University (Canada), 1981
  http://wwwlib.umi.com/dissertations/fullcit/NK52166
- **Gestural and Language Behavior of Cleft Palate and Non-Cleft Palate Children at the Age of 12 to 13 Months.** by Long, Nancy (Virginia), PhD from Northwestern University, 1979, 80 pages
  http://wwwlib.umi.com/dissertations/fullcit/7927396
- **Interaction Patterns in Cleft Palate Babies and Their Mothers** by Vagin, Anna, PhD from University of California, Berkeley with San Francisco State Univ., 1997, 103 pages
  http://wwwlib.umi.com/dissertations/fullcit/9803454
- **Mandible Growth during Palate Closure in Normal and Induced Cleft Palate in Mice** by Shih, Ling-Yu; PhD from Mcgill University (Canada), 1971
  http://wwwlib.umi.com/dissertations/fullcit/NK12039
- **Physiologic Correlates of Nasal Resonance: Aerodynamic, Radiologic, and Perceptual Studies of Normal and Cleft Palate Subjects** by Hyde, Charlene Joyce, PhD from University of California, Los Angeles, 1967, 142 pages
  http://wwwlib.umi.com/dissertations/fullcit/6800799
- **Speech Discrimination in Preschool Cleft Palate Children.** by Bonk, Mary Anne Speelman, PhD from Case Western Reserve University, 1977, 190 pages
  http://wwwlib.umi.com/dissertations/fullcit/7800552
- **Speech Intelligibility Measures of Cleft Palate Speakers before and after Pharyngeal Flap Surgery** by Shupe, Lewis Kay, PhD from State University of New York at Buffalo, 1968, 141 pages
  http://wwwlib.umi.com/dissertations/fullcit/6817345
- **The Interrelationships among Speech Acceptability, Facial Acceptability, and Self-concept of Young Adults with Cleft Palate.** by Sinko, Garnet Reynolds, PhD from The Florida State University, 1977, 131 pages
  http://wwwlib.umi.com/dissertations/fullcit/7722154
- **The Reading Cleft Palate Child** by Muller, Virginia Blow, PhD from The University of Michigan, 1982, 132 pages
  http://wwwlib.umi.com/dissertations/fullcit/8215054

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. CLINICAL TRIALS AND CLEFT PALATE

Overview

In this chapter, we will show you how to keep informed of the latest clinical trials concerning cleft palate.

Recent Trials on Cleft Palate

The following is a list of recent trials dedicated to cleft palate.[8] Further information on a trial is available at the Web site indicated.

- **Assessing the Results of Lip Surgery in Patients With Cleft Lip and Palate**

  Condition(s): Cleft Lip; Cleft Palate

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Dental and Craniofacial Research (NIDCR)

  Purpose - Excerpt: The purpose of this study is to determine whether secondary (revision) surgery to the lip in patients with cleft lip and palate is effective in improving lip function and appearance.

  Phase(s): Phase II; Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00070811

- **Cleft Palate Surgery and Speech Development**

  Condition(s): Cleft Lip; Cleft Palate

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Dental and Craniofacial Research (NIDCR); University of Sao Paulo

[8] These are listed at **www.ClinicalTrials.gov**.

Purpose - Excerpt: Compare the outcome of two primary surgeries techniques (von Langenbeck and Furlow double z-plasty) performed on children with cleft lip/palate to determine if one results in significantly better velopharyngeal competency for speech.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00004639

Keeping Current on Clinical Trials

The U.S. National Institutes of Health, through the National Library of Medicine, has developed ClinicalTrials.gov to provide current information about clinical research across the broadest number of diseases and conditions.

The site was launched in February 2000 and currently contains approximately 5,700 clinical studies in over 59,000 locations worldwide, with most studies being conducted in the United States. ClinicalTrials.gov receives about 2 million hits per month and hosts approximately 5,400 visitors daily. To access this database, simply go to the Web site at **http://www.clinicaltrials.gov/** and search by "cleft palate" (or synonyms).

While ClinicalTrials.gov is the most comprehensive listing of NIH-supported clinical trials available, not all trials are in the database. The database is updated regularly, so clinical trials are continually being added. The following is a list of specialty databases affiliated with the National Institutes of Health that offer additional information on trials:

- For clinical studies at the Warren Grant Magnuson Clinical Center located in Bethesda, Maryland, visit their Web site: **http://clinicalstudies.info.nih.gov/**
- For clinical studies conducted at the Bayview Campus in Baltimore, Maryland, visit their Web site: **http://www.jhbmc.jhu.edu/studies/index.html**
- For cancer trials, visit the National Cancer Institute: **http://cancertrials.nci.nih.gov/**
- For eye-related trials, visit and search the Web page of the National Eye Institute: **http://www.nei.nih.gov/neitrials/index.htm**
- For heart, lung and blood trials, visit the Web page of the National Heart, Lung and Blood Institute: **http://www.nhlbi.nih.gov/studies/index.htm**
- For trials on aging, visit and search the Web site of the National Institute on Aging: **http://www.grc.nia.nih.gov/studies/index.htm**
- For rare diseases, visit and search the Web site sponsored by the Office of Rare Diseases: **http://ord.aspensys.com/asp/resources/rsch_trials.asp**
- For alcoholism, visit the National Institute on Alcohol Abuse and Alcoholism: **http://www.niaaa.nih.gov/intramural/Web_dicbr_hp/particip.htm**
- For trials on infectious, immune, and allergic diseases, visit the site of the National Institute of Allergy and Infectious Diseases: **http://www.niaid.nih.gov/clintrials/**
- For trials on arthritis, musculoskeletal and skin diseases, visit newly revised site of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health: **http://www.niams.nih.gov/hi/studies/index.htm**

- For hearing-related trials, visit the National Institute on Deafness and Other Communication Disorders: **http://www.nidcd.nih.gov/health/clinical/index.htm**
- For trials on diseases of the digestive system and kidneys, and diabetes, visit the National Institute of Diabetes and Digestive and Kidney Diseases: **http://www.niddk.nih.gov/patient/patient.htm**
- For drug abuse trials, visit and search the Web site sponsored by the National Institute on Drug Abuse: **http://www.nida.nih.gov/CTN/Index.htm**
- For trials on mental disorders, visit and search the Web site of the National Institute of Mental Health: **http://www.nimh.nih.gov/studies/index.cfm**
- For trials on neurological disorders and stroke, visit and search the Web site sponsored by the National Institute of Neurological Disorders and Stroke of the NIH: **http://www.ninds.nih.gov/funding/funding_opportunities.htm#Clinical_Trials**

CHAPTER 6. BOOKS ON CLEFT PALATE

Overview

This chapter provides bibliographic book references relating to cleft palate. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, excellent sources for book titles on cleft palate 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 "cleft palate" (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 cleft palate:

- **Rehabilitation of Complex Cleft Palate and Craniomaxillofacial Defects: The Challenge of Bauru**

  Source: Carol Stream, IL: Quintessence Publishing Company, Inc. 1999. 136 p.

  Contact: Available from Quintessence Publishing Company, Inc. 551 North Kimberly Drive, Carol Stream, IL 60188-1881. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $100.00 plus shipping and handling. ISBN: 0867153474.

  Summary: Bauru is a small town in Brazil located northwest of Sao Paulo, in which there is located a clinical center for the rehabilitation of patients with congenital craniomaxillofacial deformities (particularly children with **cleft palate**). This book documents the work of an international rehabilitation team that used a method of providing surgical and prosthetic reconstruction. This method was based on a systematic approach covering transportation, accommodation, and treatment planning.

An important component of the hospital strategy was registration and continuous follow up of all patients and the results of subsequent treatment. The book offers nine chapters: the value of an integrated approach to treatment for congenital malformations of the lip and palate, prosthetic problems and solutions without osseointegrated implants, the surgical management of the adult patient with **cleft palate** and craniofacial deformities, the intraoral prosthetic aspects of bone anchored prostheses for patients with cleft palate, the clinical presentation and radiographic evaluation (intraoral case reports), postoperative follow up, extraoral bone anchored craniofacial prostheses, speech results after placement of bone anchored prostheses, and the psychological aspects of treatment with bone anchored prostheses. The text is illustrated with full color photographs.

- **Therapy Techniques for Cleft Palate Speech and Related Disorders**

  Source: San Diego, CA: Singular Publishing Group. 2001. 175 p.

  Contact: Available from Thomson Learning Group. P.O. Box 6904, Florence, KY 41022. (800) 842-3636. Fax (606) 647-5963. Website: www.singpub.com. PRICE: $49.95 plus shipping and handling. ISBN: 076930169X.

  Summary: This book describes speech therapy for individuals with **cleft palate**, velopharyngeal insufficiency (VPI), and their sequelae. The purpose of the book is to provide information that will be useful to clinicians and parents of children with '**cleft palate** speech.' The author provides a developmental approach, written in response to requests for information from speech language pathologists (SLPs) being asked to offer therapeutic services to individuals with **cleft palate** at various stages of development. The author describes the types of interventions that may be provided by speech specialists treating children with **cleft palate** and related disorders, including feeding, early intervention, prevention, and treatment, along with recommendations about when treatment should be applied. The author focuses on how SLPs can guide parents through the therapy process, not just to understand it, but to participate in that process. Ten chapters cover speech production, working with infants and toddlers with **cleft palate**, models of service delivery from preschool through adolescence, techniques for the elimination of abnormal compensatory errors, moving from sounds to conversation, procedures and materials, evaluation and therapy techniques to avoid, and velocardiofacial syndrome and other special groups. The book is illustrated with black and white photographs of SLPs and children in the therapeutic setting. The book concludes with a references list, an appendix of selected resources, and a subject index. 78 references.

- **Cleft Palate Story**

  Source: Carol Stream, IL: Quintessence Publishing Company, Inc. 1994. 239 p.

  Contact: Available from Quintessence Publishing Company, Inc. 551 North Kimberly Drive, Carol Stream, IL 60188-1881. (800) 621-0387 or (630) 682-3223; Fax (630) 682-3288; E-mail: quintpub@aol.com; http://www.quintpub.com. PRICE: $24.00 plus shipping and handling. ISBN: 0867152591.

  Summary: This book provides information for the parents of a child born with a cleft lip and/or **cleft palate**. Ten chapters guide parents through the practical issues of caring for their child. Topics covered include issues upon diagnosis, feeding the child, the anatomy of clefts, the causes of clefting, the **cleft palate** team, preparing for surgery, surgical procedures, facial and dental concerns, speech concerns, and hearing concerns. The book is written in non-technical language and illustrated throughout with drawings and

photographs to facilitate understanding. Five appendices are included: a list of financial assistance and other resources, tips on financing health care, resources for people with facial differences, a selected bibliography, and a glossary of terms. A subject index concludes the volume.

- **Cleft Palate: Interdisciplinary Issues and Treatment: For Clinicians By Clinicians**

  Source: Austin, TX: PRO-ED, Inc. 1993. 409 p.

  Contact: Available from PRO-ED, Inc. 8700 Shoal Creek Boulevard, Austin, TX 78757-6897. (800) 897-3202 or (512) 451-3246; Fax (800) 397-7633. PRICE: $36.00 plus shipping and handling. ISBN: 0890795673.

  Summary: This book, written primarily for speech language pathologists and audiologists, presents an interdisciplinary approach to the diagnosis and treatment of cleft lip and palate. Twelve chapters cover topics including the interdisciplinary team approach, the development and genetic aspects of cleft lip and palate, surgical issues and procedures, oral and maxillofacial surgery and the management of cleft lip and palate, orthodontic diagnosis and treatment procedures, the prosthodontic management of maxillofacial and palatal defects, otologic and audiologic concerns and treatment, early phonological development and the child with **cleft palate**, the evaluation of velopharyngeal function, articulation assessment procedures and treatment decisions, behavioral approaches to treating velopharyngeal closure and nasality, and psychological characteristics associated with **cleft palate**. Each chapter includes extensive references and black and white photographs where appropriate. Author and subject indices conclude the volume.

- **Cleft Palate Speech Management: A Multidisciplinary Approach**

  Source: St. Louis, MO: Mosby-Year Book, Inc. 1995. 400 p.

  Contact: Available from Mosby-Year Book, Inc. 11830 Westline Industrial Drive, St. Louis, MO 63146-3318. (800) 633-6699; Fax (800) 535-9935. PRICE: $61.95 plus shipping and handling. ISBN: 0801664470.

  Summary: This textbook provides direct instruction to speech pathologists for managing patients with clefts. Disorders of communication related to cleft lip and palate are emphasized in terms of the authors' clinical approach and the method of finding solutions to various problems in the treatment of children and adults with clefts. The book includes descriptions of diagnostic and treatment protocols, the rationales for using them, the complications of various treatments, and the advantages of specific procedures applied to thousands of patients. The text emphasizes the interdisciplinary management of patients with clefts. Seventeen chapters cover the genetics of clefting and associated syndromes, anatomy and physiology, pediatric care and feeding, complications associated with clefting and craniofacial disorders, cleft classification and cleft lip repair, **cleft palate** repair, communicative impairment associated with clefting, the evaluation and remediation of language impairment, the evaluation of speech disorders associated with clefting, the instrumental assessment of velpharyngeal valving, orthodontic treatment of children with cleft lip and palate, the dynamics of speech and orthodontic managment, treatment of articulation and resonance disorders, and speech bulbs. A detailed subject index concludes the volume.

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 "cleft palate" at online booksellers' Web sites, you may discover non-medical books that use the generic term "cleft palate" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "**cleft palate**" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **A Cleft Palate Team Addresses the Speech Clinician.** by Ill., Thomas [1971 Springfield; ISBN: 0398005427; http://www.amazon.com/exec/obidos/ASIN/0398005427/icongroupinterna
- **A Curriculum for Infants and Toddlers With Cleft Palate**; ISBN: 9991625755; http://www.amazon.com/exec/obidos/ASIN/9991625755/icongroupinterna
- **A Curriculum for Infants and Toddlers With Cleft Palate: Developing Speech and Language** by Joan I. Lynch, et al; ISBN: 9993782394; http://www.amazon.com/exec/obidos/ASIN/9993782394/icongroupinterna
- **Advances in the Management of Cleft Palate** by M. Edwards (Editor); ISBN: 0443016011; http://www.amazon.com/exec/obidos/ASIN/0443016011/icongroupinterna
- **Advice to Parents of a Cleft Palate Child** by Donna Konkel, M.A. Wicka, Mervyn L. Falk (Contributor); ISBN: 0398047049; http://www.amazon.com/exec/obidos/ASIN/0398047049/icongroupinterna
- **Analyzing Cleft Palate Speech** by Pamela Grunwell (Editor); ISBN: 156593251X; http://www.amazon.com/exec/obidos/ASIN/156593251X/icongroupinterna
- **Atlas of Cleft Lip and Cleft Palate Surgery** by Howard W. Smith, David M. Bolinsky; ISBN: 0808915932; http://www.amazon.com/exec/obidos/ASIN/0808915932/icongroupinterna
- **Cleft Palate** by Harold Westlake; ISBN: 0131362593; http://www.amazon.com/exec/obidos/ASIN/0131362593/icongroupinterna
- **Cleft Palate (Pro-Ed Studies in Communicative Disorders)** by Gene R. Powers; ISBN: 0890790949; http://www.amazon.com/exec/obidos/ASIN/0890790949/icongroupinterna
- **Cleft palate and associated speech characteristics** by Raymond Massengill; ISBN: 0822018012; http://www.amazon.com/exec/obidos/ASIN/0822018012/icongroupinterna
- **Cleft Palate and Cleft Lip: A Team Approach to Clinical Management and Rehabilitation of the Patient** by Herbert K., Sr., Cooper; ISBN: 0721626874; http://www.amazon.com/exec/obidos/ASIN/0721626874/icongroupinterna
- **Cleft Palate and Craniofacial Anomalies: Effects on Speech and Resonance** by Ann W. Kummer; ISBN: 0769300774; http://www.amazon.com/exec/obidos/ASIN/0769300774/icongroupinterna

- **Cleft Palate and Its Associated Speech Disorders** by Charlotte G. Wells; ISBN: 0070692432;
  http://www.amazon.com/exec/obidos/ASIN/0070692432/icongroupinterna
- **Cleft Palate and Other Maxillofacial Disorders** by Jeri A. Logemann (Editor); ISBN: 0316530824;
  http://www.amazon.com/exec/obidos/ASIN/0316530824/icongroupinterna
- **Cleft Palate and Related Disorders** by Grace Middleton; ISBN: 1883315255;
  http://www.amazon.com/exec/obidos/ASIN/1883315255/icongroupinterna
- **Cleft Palate and Speech** by Muriel E. Morley; ISBN: 0443006970;
  http://www.amazon.com/exec/obidos/ASIN/0443006970/icongroupinterna
- **Cleft Palate Children and Intelligence** by J. A. Heineman-De Boer; ISBN: 9026506058;
  http://www.amazon.com/exec/obidos/ASIN/9026506058/icongroupinterna
- **Cleft Palate Deformation: Causation and Prevention,** by J. J. Longacre; ISBN: 0398011427;
  http://www.amazon.com/exec/obidos/ASIN/0398011427/icongroupinterna
- **Cleft Palate Dentistry** by Robert E. McKinstry; ISBN: 1886236070;
  http://www.amazon.com/exec/obidos/ASIN/1886236070/icongroupinterna
- **Cleft Palate Sourcebook** by Liz Albery, Jane Russell; ISBN: 0863881270;
  http://www.amazon.com/exec/obidos/ASIN/0863881270/icongroupinterna
- **Cleft Palate Speech** by Sally J., PhD Peterson-Falzone, et al; ISBN: 0815131534;
  http://www.amazon.com/exec/obidos/ASIN/0815131534/icongroupinterna
- **Cleft Palate Speech Management: A Multidisciplinary Approach** by Robert J. Shprintzen, Janusz Bardach; ISBN: 0801664470;
  http://www.amazon.com/exec/obidos/ASIN/0801664470/icongroupinterna
- **Cleft Palate, Middle Ear Disease, and Hearing Loss** by Malcolm D. Graham; ISBN: 0398036675;
  http://www.amazon.com/exec/obidos/ASIN/0398036675/icongroupinterna
- **Cleft Palate: Interdisciplinary Issues and Treatment (For Clinicians by Clinicians)** by Karlind T. Moller, Clark D. Starr (Editor); ISBN: 0890795673;
  http://www.amazon.com/exec/obidos/ASIN/0890795673/icongroupinterna
- **Cleft Palate: The Nature and Remediation of Communication Problems** by Jackie Stengelhofen Dip CST DTST MEd MCST (Editor); ISBN: 1897635052;
  http://www.amazon.com/exec/obidos/ASIN/1897635052/icongroupinterna
- **Cleft Palate: The Nature and Remediation of Communication Problems** by Jackie Stengelholfen (Editor); ISBN: 0443038694;
  http://www.amazon.com/exec/obidos/ASIN/0443038694/icongroupinterna
- **Diagnosing Speech Disorders from Cleft Palate** by Samuel Glen Fletcher; ISBN: 0808910744;
  http://www.amazon.com/exec/obidos/ASIN/0808910744/icongroupinterna
- **Etiology of Cleft Lip and Cleft Palate** by Michael Melnick, et al; ISBN: 0471615722;
  http://www.amazon.com/exec/obidos/ASIN/0471615722/icongroupinterna
- **Etiology of cleft lip and cleft palate : proceedings of a workshop held at Airlie House, Virginia, sponsored by the National Institute of Dental Research and the Society of Craniofacial Genetics**; ISBN: 0845100467;
  http://www.amazon.com/exec/obidos/ASIN/0845100467/icongroupinterna

- **Living With Disfigurement: Psychological Implications of Being Born With a Cleft Palate (Cedr)** by Poppy Nash; ISBN: 1856289672; http://www.amazon.com/exec/obidos/ASIN/1856289672/icongroupinterna
- **Parents' Guide to Cleft Palate Habilitation; The Team Approach** by Aaron H. Bleiberg; ISBN: 0682471836; http://www.amazon.com/exec/obidos/ASIN/0682471836/icongroupinterna
- **Psychosocial aspects of the "cleft palate problem"** by D. C. Spriestersbach; ISBN: 0877450374; http://www.amazon.com/exec/obidos/ASIN/0877450374/icongroupinterna
- **Rehabilitation of Complex Cleft Palate and Craniomaxillofacial Defects: The Challenge of Bauru** by Per-Ingvar Branemark (Editor), et al; ISBN: 0867153474; http://www.amazon.com/exec/obidos/ASIN/0867153474/icongroupinterna
- **Speech Language and Psycholocial Aspects of Cleft Lip and Cleft Palate: The State of the Art**; ISBN: 9995847507; http://www.amazon.com/exec/obidos/ASIN/9995847507/icongroupinterna
- **The Bratislava project : some results of cleft palate surgery**; ISBN: 0877450757; http://www.amazon.com/exec/obidos/ASIN/0877450757/icongroupinterna
- **The Cleft Palate Experience: New Perspectives on Management** by Edward Clifford; ISBN: 0398053030; http://www.amazon.com/exec/obidos/ASIN/0398053030/icongroupinterna
- **The Cleft Palate Story** by Samuel Berkowitz; ISBN: 0867152591; http://www.amazon.com/exec/obidos/ASIN/0867152591/icongroupinterna
- **Therapy Techniques for Cleft Palate Speech and Related Disorders** by Karen J. Golding-Kushner, Karen Golding Kushner; ISBN: 076930169X; http://www.amazon.com/exec/obidos/ASIN/076930169X/icongroupinterna
- **Transactions 8th International Congress on Cleft Palate and Related Craniofacial Anomalies**; ISBN: 9810095198; http://www.amazon.com/exec/obidos/ASIN/9810095198/icongroupinterna
- **Videofluoroscopic Studies of Speech in Patients With Cleft Palate** by M. Leon Skolnick, et al; ISBN: 0387969586; http://www.amazon.com/exec/obidos/ASIN/0387969586/icongroupinterna

Chapters on Cleft Palate

In order to find chapters that specifically relate to cleft palate, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and cleft palate 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 "cleft palate" (or synonyms) into the "For these words:" box. The following is a typical result when searching for book chapters on cleft palate:

- **Oral Care for Children with Cleft Lip or Cleft Palate**

  Source: in Sutton, A.L. Dental Care and Oral Health Sourcebook. 2nd ed. Detroit, MI: Omnigraphics. 2003. p. 393-400.

  Contact: Available from Omnigraphics. 615 Griswold Street, Detroit, MI 48226. (313) 961-1340. Fax: (313) 961-1383. E-mail: progers@omnigraphics.com. www.omnigraphics.com. PRICE: $78.00; plus shipping and handling. ISBN: 780806344.

  Summary: A cleft lip is a separation of the two sides of the lip. The separation often includes the bones of the upper jaw or upper gum. A **cleft palate** is an opening in the roof of the mouth in which the two sides of the palate did not fuse as the unborn baby was developing. This chapter on oral care for children with cleft lip or **cleft palate** is from a book that provides information about dental care and oral health at all stages of life. Topics include how cleft lip or palate affects the teeth, early dental care, proper tooth cleaning, good nutrition, the use of fluoride, orthodontic care, coordinated dental and surgical care, prosthodontic care, missing teeth in children with cleft lip or **cleft palate**, the members of the patient care team, options for the permanent replacement of the lateral incisor, and options for a patient who has had a bone graft. 2 figures.

- **Surgical Management of the Adult Patient with Cleft Palate and Craniofacial Deformities**

  Source: in Branemark, P.; Higuchi, K.W.; de Oliveira, M.F., eds. Rehabilitation of Complex Cleft Palate and Craniomaxillofacial Defects: The Challenge of Bauru. Carol Stream, IL: Quintessence Publishing Company, Inc. 1999. p. 13-20.

  Contact: Available from Quintessence Publishing Company, Inc. 551 North Kimberly Drive, Carol Stream, IL 60188-1881. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $100.00 plus shipping and handling. ISBN: 0867153474.

  Summary: Bauru is a small town in Brazil, located northwest of Sao Paulo, in which there is located a clinical center for the rehabilitation of patients with congenital craniomaxillofacial deformities (particularly children with **cleft palate**). This chapter is from a book that documents the work of an international rehabilitation team that used a method of providing surgical and prosthetic reconstruction. This method was based on a systematic approach covering transportation, accommodation, and treatment planning. An important component of the hospital strategy was registration and continuous follow up of all patients and the results of subsequent treatment. This chapter discusses the surgical management of the adult patient with **cleft palate** and craniofacial deformities. The authors describe various surgical considerations unique to the treatment of 14 adult cleft patients and nine additional patients receiving implant retained facial prostheses and bone anchored hearing aids. Topics include the classification of bone grafting for the patient with **cleft palate**, residual adult cleft problems, team organization, treatment planning, presurgical considerations, surgical methodology for tertiary grafting (osseointegration surgery), and surgical methodology for craniofacial defect rehabilitation. The authors conclude with a brief discussion of cost and time factors, noting that it is not possible to completely measure the functional and psychosocial improvement derived by patients receiving treatment. This was especially true of the patients with the most severe cleft and facial defect anatomy, among whom postoperative satisfaction was uniformly reported. 20 references.

- **Pathological Anatomy and Physiology in Isolated Cleft Palate**

  Source: in Malek, R. Cleft Lip and Palate: Lesions, Pathophysiology and Primary Treatment. London, England: Martin Dunitz Ltd. 2001. p.121-130.

  Contact: Available from Martin Dunitz Ltd, The Livery House. 7-9 Pratt Street, London, England NW1 0AE. 4404074822202. Website: www.dunitz.co.uk. Email: info@mdunitz.globalnet.co.uk. PRICE: $150.00 plus shipping and handling. ISBN: 1853174912.

  Summary: This chapter is from a text that offers an update on the lesions, pathophysiology, and primary treatment of cleft lip and palate. Each chapter of the book includes a study of anatomical pathology preceded by a background refresher on normal anatomy. In this chapter, the author covers the pathological anatomy and physiology in isolated **cleft palate**. Topics include bone structure; muscles and mucosa; the physiopathology of the **cleft palate**; sucking or swallowing disorders; associated respiratory disorders; the physiology of the Eustachian tube and how it can be impaired by the gap in the palate; related speech disorders; and velopharyngeal incompetence (when the soft palate cannot fulfills its role in closing the nasopharynx and speech is subsequently seriously affected). 9 figures.

- **Cleft Lip and Cleft Palate**

  Source: in Vinson, B.P. Essentials for Speech-Language Pathologists. San Diego, CA: Singular Publishing Group. 2001. p. 179-202.

  Contact: Available from Thomson Learning Group. P.O. Box 6904, Florence, KY 41022. (800) 842-3636. Fax (606) 647-5963. Website: www.singpub.com. PRICE: $49.95 plus shipping and handling. ISBN: 0769300715.

  Summary: This chapter on cleft lip and **cleft palate** is from a textbook that is designed to help new professionals with the transition to clinical practice in speech language pathology. The author describes and defines the condition and emphasizes the importance of a comprehensive, multidisciplinary approach to the care of a child with a cleft. The author notes that cleft lip and palate are associated with over 350 syndromes, and more than 50 percent of children with **cleft palate** only are likely to have developmental deficits or other associated malformations. The author discusses velo cardio facial syndrome (VCFS); velopharyngeal function; assessment issues, including the oral facial examination, oral health in children with cleft lip and palate, voice, language, speech (hypernasality and nasal emission, compensatory articulation strategies, modified tongue anchor procedure, and cul de sac resonance), and acoustic measures; and treatment considerations, divided by age groups (immediately after birth, first year, second year, third year, etc., through early adolescence), including feeding, pharyngeal flap, the nonsurgical treatment of hypernasality, social emotional development, and issues relating to school age children (including adolescents). One appendix offers a checklist for the assessment of clients with clefts.

- **Getting an Early Start: Infants and Toddlers with Cleft Palate**

  Source: in Golding-Kushner, K.J. Therapy Techniques for Cleft Palate Speech and Related Disorders. San Diego, CA: Singular Publishing Group. 2001. p. 35-60.

  Contact: Available from Thomson Learning Group. P.O. Box 6904, Florence, KY 41022. (800) 842-3636. Fax (606) 647-5963. Website: www.singpub.com. PRICE: $49.95 plus shipping and handling. ISBN: 076930169X.

Summary: This chapter on infants and toddlers with **cleft palate** is from a book that describes speech therapy for individuals with **cleft palate**, velopharyngeal insufficiency (VPI), and their sequelae. The purpose of the book is to provide information that will be useful to clinicians and parents of children with '**cleft palate** speech.' In this chapter, the author notes that the first contact between speech language pathologists (SLPs) and the family of a baby with **cleft palate** often occurs in the newborn period because of feeding concerns. In most cases, minor adjustments in positioning of the baby and the nipple are successful in establishing a normal feeding routine. The author also discusses early intervention, home programs, and the prevention of compensatory errors. Specific topics include feeding and oral motor skills, speech therapy for babies, language development, models of service delivery, prevention of speech and language disorders, home programs for early intervention, eliciting oral sound production in very young children, the nasal escape of air and hypernasality, recognizing first word attempts, prevention of glottal stop errors, when to ignore speech and when to start direct therapy. Parents should be reminded to follow up with medical care, especially because of the high frequency of middle ear disease among children with **cleft palate**. 5 figures. 4 tables.

- **Cleft Palate Team**

  Source: in Berkowitz, S. The Cleft Palate Story. Carol Stream, IL: Quintessence Publishing Company, Inc. 1994. p. 51-60.

  Contact: Available from Quintessence Publishing Company, Inc. 551 North Kimberly Drive, Carol Stream, IL 60188-1881. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $24.00 plus shipping and handling. ISBN: 0867152591.

  Summary: This chapter on the **cleft palate** team is from a handbook that provides practical information for the parents of a child born with a cleft lip and/or **cleft palate**. Topics include the first team evaluation on a baby born with a cleft; the role of each member of the **cleft palate** team, which can include plastic surgeon, speech pathologist, orthodontist, oral and maxillofacial surgeon, psychologist, geneticist, radiologist, social worker, public health nurse, and pediatrician; striking a balance between local care and specialized care at major centers; the parental role on the **cleft palate** team; and the role of the psychologist and social worker. The chapter concludes with a list and brief description of the more common diagnostic procedures, tests, and instruments used by **cleft palate** teams to assess the overall condition and development of children with clefts. One sidebar presents a list of concepts from the parents' perspective for professionals to keep in mind. The chapter is written in non-technical language to facilitate understanding.

- **Therapy Considerations for Preschool Age Children with Cleft Palate**

  Source: in Bzoch, K.R., ed. Communicative Disorders Related to Cleft Lip and Palate. 4th ed. Austin, TX: PRO-ED, Inc. 1997. p. 475-491.

  Contact: Available from PRO-ED, Inc. 8700 Shoal Creek Boulevard, Austin, TX 78757-6897. (512) 451-3246. Fax (800) 397-7633. PRICE: $56.70 plus shipping and handling. ISBN: 0890797013.

  Summary: This chapter on therapy considerations for preschool age children with **cleft palate** is from a textbook that explores cleft lip and **cleft palate** and the communicative disorders that can result from these conditions. The author considers the interaction of various elements that influence the clinician's professional concerns for these preschool

clients. Critical elements unique to care of clients with **cleft palate** in this age group include basic knowledge about the normal growth and development of preschoolers, preschool differences related to **cleft palate**, and clinical decision making. The author presents four detailed case studies to illustrate the concepts of care for this population. The author concludes that, especially for preschool children with **cleft palate** and other speech, language and hearing disorders, the lack of stimulation and reinforcement for good communication skills puts them at risk of developing unnecessary disorders and threatens the good skills learned in earlier therapies. 1 figure. 44 references.

Directories

In addition to the references and resources discussed earlier in this chapter, a number of directories relating to cleft palate 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:[9]

- **Parent Resources: Agencies, Organizations, Support Groups**

  Source: in DeFeo, A.B., ed. Parent Articles 2. San Antonio, TX: Communication Skill Builders. 1995. p. 213-234.

  Contact: Available from Communication Skill Builders. Customer Service, 555 Academic Court, San Antonio, TX 78204-2498. (800) 211-8378; Fax (800) 232-1223. PRICE: $55.00 plus shipping and handling. Order Number 076-163-0732.

  Summary: This appendix section is from a parent education skill builders textbook. The appendix lists agencies, organizations, and support groups that parents might want to contact as they work with developing communication skills in and with their child. National information and advocacy groups are listed, including groups for consumer information, education, financial aid, home care, legal assistance, nonoral communication, orthotics and prosthetics, psychiatry, psychology, rare disorders, rehabilitation, residential placement, self-help, severe disabilities, sibling support, social workers, and telephone usage for persons with disabilities. Also listed are national organizations for specific disabilities and conditions, including acoustic neuroma, autism, birth defects, chronic dizziness and balance disorders, **cleft palate** and craniofacial disorders, developmental disabilities, Down's syndrome, dyslexia, dystonia, genetic conditions, head injuries, hearing impairments, learning disabilities, mental retardation, neurofibromatosis, neurological disorders, stuttering, Tourette syndrome, and voice disorders and laryngectomies. The address and telephone number for each organization are noted.

- **Self-Help Sourcebook: Finding and Forming Mutual Aid Self-Help Groups. 4th ed**

  Source: Denville, NJ: American Self-Help Clearinghouse. 1992. 226 p.

  Contact: Available from American Self-Help Clearinghouse. Attn: Sourcebook, St. Clares-Riverside Medical Center, 25 Pocono Road, Denville, NJ 07834. Voice (201) 625-

[9] You will need to limit your search to "Directory" and "cleft palate" 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 "cleft palate" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months.

7101; TTY (201) 625-9053. PRICE: $9.00 book rate; $10.00 first class mail. ISBN: 0963432206.

Summary: This sourcebook lists self-help groups in a wide variety of topic areas, including addictions and dependencies, bereavement, disabilities, health, mental health, parenting and family, physical and/or emotional abuse, and miscellaneous categories. Topics relevant to deafness and communication disorders include acoustic neuroma, alternative/augmentative communication, autism, **cleft palate** and cleft lip, cochlear implants, developmental disabilities, developmentally delayed children, Down syndrome, dystonia, ear anomalies, elective mutism, hearing impairment, inner ear problems, laryngectomy, late-deafened adults, learning disabilities, Meniere's disease, neck-head-oral cancer, parents of children with hearing impairment, speech dysfunction, speech impairments, stuttering, tinnitus, Tourette syndrome, and Usher's syndrome. In addition to basic information about the self-help groups, the sourcebook lists self-help clearinghouses, toll-free helplines, resources for rare disorders, resources for genetic disorders, housing and neighborhood resources and resources for the homeless, how-to ideas for developing self-help groups, and using a home computer for mutual help. The book includes a bibliography and key word index.

CHAPTER 7. MULTIMEDIA ON CLEFT PALATE

Overview

In this chapter, we show you how to keep current on multimedia sources of information on cleft palate. 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 cleft palate is the Combined Health Information Database. You will need to limit your search to "Videorecording" and "cleft palate" 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 "cleft palate" (or synonyms) into the "For these words:" box. The following is a typical result when searching for video recordings on cleft palate:

- **Operation: Cleft Palate Reconstruction**

  Source: Princeton, NJ: Films for the Humanities and Sciences. 1995. (videocassette).

  Contact: Available from Films for the Humanities and Sciences. P.O. Box 2053, Princeton, NJ 08543-2053. (800) 257-5126 or (609) 275-1400. Fax (609) 275-3767. E-mail: custserv@films.com. Website: www.films.com. PRICE: $149.00 plus shipping and handling. Item number BVL 6264.

  Summary: **Cleft palate** is considered the most common birth defect among white Americans. This videotape program follows a young child in need of a **cleft palate** reconstruction. The child had an initial operation to repair his lip when he was three months old. Now eleven months old, the child undergoes the second operation to repair his cleft. The videotape program follows the child through the preoperative care, the surgery itself, and the postoperative care and results. The narration provides explanations of the medical concepts and techniques used.

- **Cleft palate - craniofacial anomalies: Information for primary care physicians, nurses, case managers, dentists, and speech-language pathologists and audiologists**

  Source: Pittsburgh, PA: American Cleft Palate - Craniofacial Association. ca. 1994. 5 videotapes (VHS, color, 22 minutes).

  Contact: Available from American Cleft Palate/Craniofacial Association, 1218 Grandview Avenue, Pittsburgh, PA 15211. Telephone: (412) 481- 1376.

  Summary: This set of videotapes provides an overview of cleft lip, **cleft palate**, and other craniofacial anomalies, and discusses related problems that can occur, how to advise parents, the health care team, and services needed by individuals with these disorders. They also discuss a related publication by the association on parameters for evaluation and treatment of these disorders, and other services of the association. Each videotape is aimed at a separate group of health care professionals: primary care physicians, nurses, case managers, dentists, and speech-language pathologists and audiologists. [Funded by the Maternal and Child Health Bureau].

- **Early speech intervention for children with cleft palate: An outreach training guide for community-based speech-language pathologists**

  Source: Portland, OR: Child Development and Rehabilitation Center, Oregon Health Sciences University. 1995. 61 pp.

  Contact: Available from Publications, Oregon Health Sciences University, Child Development and Rehabilitation Center, P.O. Box 574, Portland, OR 97207-0574. Telephone: (800) 452-3563, ext. 7634 or (503) 494-4219. $60.00 includes shipping and handling.

  Summary: This training guide is designed to review and update information for the community-based speech-language pathologist on the nature of **cleft palate** and the design and implementation of treatment programs for young children ages 2-1/2 to 5. The goal is to assist practitioners in helping young children, by the time they are ready to enter school, achieve developmentally normal articulation, normalized voice quality, nasal resonance balance, and normal hearing for educational purposes. [Funded by the Maternal and Child Health Bureau].

CHAPTER 8. PERIODICALS AND NEWS ON CLEFT PALATE

Overview

In this chapter, we suggest a number of news sources and present various periodicals that cover cleft palate.

News Services and Press Releases

One of the simplest ways of tracking press releases on cleft palate 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 "cleft palate" (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 cleft palate. 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 "cleft palate" (or synonyms). The following was recently listed in this archive for cleft palate:

- **UK curate in court over cleft palate baby abortion**
  Source: Reuters Health eLine
  Date: December 01, 2003
- **Folate-rich diet may cut cleft palate risk**
  Source: Reuters Health eLine
  Date: April 04, 2003

- **Genetic basis of cleft palate deformities clarified**
  Source: Reuters Medical News
  Date: September 17, 2001
- **Gene mutation linked to cleft lip, cleft palate**
  Source: Reuters Health eLine
  Date: August 01, 2000
- **Disruption of TGF-alpha function proposed as key to development of cleft palate**
  Source: Reuters Medical News
  Date: May 03, 1999
- **Broken Gene Circuit May Cause Cleft Palate**
  Source: Reuters Health eLine
  Date: December 30, 1997
- **Folic Acid Supplementation During Pregnancy May Prevent Cleft Lip And Cleft Palate In Offspring**
  Source: Reuters Medical News
  Date: August 11, 1995
- **Maternal Smoking Linked To Cleft Palate In Offspring**
  Source: Reuters Medical News
  Date: April 04, 1995

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 "cleft palate" (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 "cleft palate" (or synonyms). If you know the name of a company that is relevant to cleft palate, 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 "cleft palate" (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 "cleft palate" (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 cleft palate:

- **Treatment Complexities of the Turner's Syndrome Patient**

  Source: Oral-B Case Studies in Dental Hygiene. 1(1): 1-4,6-8. Summer 2003.

  Contact: Available from Oral-B Case Studies in Dental Hygiene, Professional Audience Communications, Inc. P.O. Box 243, Yardley, PA 19067. (800) 446-7252. Website: www.oralb.com/dentalpros.

  Summary: Effective patient assessment is critical to the delivery of high quality dental hygiene care. This article helps dental hygienists understand the treatment complexities of working with patients with Turner's syndrome, a complex medical condition characterized by oral, physical, and psychological features. Common physical characteristics of Turner's syndrome patients include short stature, webbed neck, and hypoplastic pinna (underdeveloped outer ears), underdeveloped or shield chest with wide-spaced nipples, and edema of the hands and feet. Oral features associated with Turner's syndrome include high arched and narrow palate, occurrence of **cleft palate** at higher-than-normal frequency, significantly smaller mesio-distal dimensions of the teeth, bifurcated roots and reduced root length, particularly in the maxilla (upper jaw), premature tooth eruption, increased molarization of premolars, and the presence of hypoplasia. The article then describes a case of the management of a patient diagnosed with Turner's syndrome. The young woman (age 21 years) presented with severe retrognathia, posterior open bite, crossbite on the right side, generalized enamel hypoplasia, shortened roots, thin dentin, compromised dexterity, osteoporosis, mitral valve prolapse, and low self-esteem. The dentist and dental hygienist provided this

patient with comprehensive care in consultation with the patient's physician and other dental specialists. A posttest with which readers can obtain continuing education credit is appended to the article. 5 figures. 2 tables. 29 references.

- **Single vs Two Stage Palatal Closure**

  Source: Cleft Palate Reflections. p. 1-2, 4. Spring 1993.

  Contact: Available from Shadyside Maxillofacial and Cleft Palate Prosthetic Center. Shadyside Medical Center, Suite 207, 5200 Centre Avenue, Pittsburgh, PA 15232. (412) 621-4310.

  Summary: This article is from a newsletter designed to provide information to **cleft palate** patients, parents, and health care providers on **cleft palate** treatment teams. The article stresses that the goals of cleft lip and palate treatment include the establishment of normal speech, normal appearance, and normal occlusion. In order to avoid restricting the growth of the maxilla, delayed closure of the hard and soft palate has been proposed by several surgeons. Several practitioners have suggested that the scar band formed in a single-stage closure can produce a functional ankylosis (restriction) in the normal forward growth of the maxilla and middle of the face. In a two-stage palatal repair, the soft palate is usually repaired before the hard palate. The hard palate may be left open, closed (obturated) by a removable prosthesis when a sufficient number of teeth are present for retention of the prosthesis, or closed by a pin-retained prosthesis. When the hard palate is left open for several years, speech defects have been reported. A single-stage closure involves surgically repairing both the hard and soft palate in one operation. This procedure, usually done around 18 months of age, allows for the development of speech with a completely intact soft and hard palate. The author concludes that since abnormal speech is the major problem for patients with **cleft palates,** it may be more advantageous to close the hard and soft palate in a single-stage closure. 1 figure.

- **Premaxillary Orthopedics**

  Source: Cleft Palate Reflections. p. 1-2, 4. Summer 1993.

  Contact: Available from Shadyside Maxillofacial and Cleft Palate Prosthetic Center. Shadyside Medical Center, Suite 207, 5200 Centre Avenue, Pittsburgh, PA 15232. (412) 621-4310.

  Summary: This article on premaxillary orthopedics is from a newsletter for **cleft palate** patients, parents, and health care providers on **cleft palate** treatment teams. Maxillary orthopedics in **cleft palate** patients involves the repositioning of the maxillary bony segments to produce a normal skeletal base under the lip and nose. This orthopedic intervention is usually undertaken in the first several weeks of the **cleft palate** individual's life and may be continued until surgical closure of the hard and soft palate is done at 18 to 24 months of age. The author explores the controversies surrounding premaxillary orthopedics in **cleft palates,** presenting both sides of the issue of whether or not the procedure is necessary. The author concludes that premaxillary orthopedics is not indicated in every case. Close cooperation and communication between the plastic surgeon and the dental specialist is needed to insure clinical success. The article concludes with a delineation of the steps commonly taken in the premaxillary orthopedic procedure. 4 figures.

- **Premaxillary Orthopedic: Unilateral Cleft Lip and Palate**

  Source: Cleft Palate Reflections. p. 1-2, 4. Fall 1993.

  Contact: Available from Shadyside Maxillofacial and Cleft Palate Prosthetic Center. Shadyside Medical Center, Suite 207, 5200 Centre Avenue, Pittsburgh, PA 15232. (412) 621-4310.

  Summary: This article on the use of premaxillary orthopedics in unilateral cleft lip and palate is from a newsletter for **cleft palate** patients, parents, and health care providers on **cleft palate** treatment teams. After a description of the differences between a unilateral and bilateral cleft, the author considers whether premaxillary orthopedics need to be performed in every unilateral cleft lip and palate case. The author notes that premaxillary orthopedics is not indicated in many of these patients. When the cleft is narrow, the surgical repair of the lip is sufficient to mold the major segment towards the minor segment, producing a symmetrical dental arch. However, in the subgroup of unilateral cleft lip and palate patients that have wide clefts (i.e., 10 to 20 mm in width), there may be a role for premaxillary orthopedic treatment. The objective of premaxillary orthopedic treatment is to reduce the width of the cleft by overcoming the lateral pull of the facial muscles and preventing the tongue from resting in the cleft. Care must be taken to prevent collapse of the cleft segments during treatment by overzealous extraoral traction. The article concludes with a discussion of three common ways to perform premaxillary orthopedic treatment: extraoral strapping alone, extraoral strapping with an intraoral appliance, and the use of a Latham appliance. 5 figures.

- **Latham Appliances**

  Source: Cleft Palate Reflections. p. 1-2, 4. Summer 1994.

  Contact: Available from Shadyside Maxillofacial and Cleft Palate Prosthetic Center. Shadyside Medical Center, Suite 207, 5200 Centre Avenue, Pittsburgh, PA 15232. (412) 621-4310.

  Summary: This article on the use of the Latham appliance in premaxillary orthopedics in cleft lip and palate is from a newsletter for **cleft palate** patients, parents, and health care providers on **cleft palate** treatment teams. Latham appliances are pin retained appliances designed to move the cleft maxillary segments forward (unilateral clefts) or the premaxilla backwards (bilateral clefts). This movement of the cleft segments forward tends to improve the base of the nose, which makes for an easier surgical reconstruction of the nose and initial closure of the lip. The author describes the development of the Latham appliances, their indications, and problems that may be encountered with their use. The author concludes that Latham appliances have a use in premaxillary orthopedics; however, every patient with cleft lip and palate does not require premaxillary orthopedics. 4 figures.

- **Management of the Cleft Lip-Palate Patient**

  Source: AAOMS Surgical Update. p. 1-6. Winter 1992.

  Contact: Available from American Association of Oral and Maxillofacial Surgeons (AAOMS). Committee on Public Information, 9700 West Bryn Mawr Avenue, Rosemont, IL 60018-5701. (800) 366-6725 or (847) 678-6200; Fax (847) 678-6286 or (630) 241-9805; http://www.aaoms.org.

  Summary: This issue of Surgical Update examines the types of cleft conditions and available treatment regimens, and offers guidelines for dealing with some of the special

challenges confronting the dentist and the cleft team. Topics include the diagnostic classification of cleft lip and palate; dentofacial considerations in the infant; pre-primary dentition, primary dentition, mixed dentition, and permanent dentition; surgical orthodontics; treating patients who did not experience early and continuous dental intervention, who present with various dental problems; and controversial issues in this area, including timing for total **cleft palate** closure and the real benefits of early maxillofacial orthopedic treatment. The author conclude that a coordinated team effort, which provides the earliest possible diagnosis, preventive and treatment regimens with ongoing evaluation and maintenance, can vastly improve function, esthetics, and overall quality of life for these patients. 8 figures.

- **Clefts of the Lip and Palate**

  Source: Faces. 8(2): no page nos. Spring 1994.

  Contact: Available from National Association for the Craniofacially Handicapped. P.O. Box 11082, Chattanooga, TN 37401. (615) 266-1632 or (800) 332-2373.

  Summary: This newsletter article provides an overview of clefts of the lip and palate, relatively common birth defects occurring in both males and females of all races. Topics covered include unilateral cleft lip; bilateral cleft lip; **cleft palate;** and late cleft treatment. The author focuses on the surgical correction of lip and palate clefts, stressing the important role of the craniofacial team in diagnosis and treatments of these anomalies. Photographs of four children before and after reconstructive surgery are included.

Academic Periodicals covering Cleft Palate

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to cleft palate. In addition to these sources, you can search for articles covering cleft palate 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."

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[10]:

- 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/**

[10] 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.[11] 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:[12]

- **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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[11] 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**).

[12] 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[13]

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.[14] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "cleft palate" (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	13469
Books / Periodicals / Audio Visual	312
Consumer Health	130
Meeting Abstracts	2
Other Collections	548
Total	14461

HSTAT[15]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[16] 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.[17] Simply search by "cleft palate" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

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[13] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

[14] 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).

[15] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.

[16] The HSTAT URL is **http://hstat.nlm.nih.gov/**.

[17] 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[18]

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.[19] 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.[20] 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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[18] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

[19] 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.

[20] 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 cleft palate 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 cleft palate. 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 cleft palate. 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 "cleft palate":

- Guides on cleft palate

  Cleft Lip and Palate
  http://www.nlm.nih.gov/medlineplus/cleftlipandpalate.html

- Other guides

  Birth Defects
  http://www.nlm.nih.gov/medlineplus/birthdefects.html

  Choosing a Doctor or Health Care Service
  http://www.nlm.nih.gov/medlineplus/choosingadoctororhealthcareservice.html

  Facial Injuries and Disorders
  http://www.nlm.nih.gov/medlineplus/facialinjuriesanddisorders.html

  Head and Brain Malformations
  http://www.nlm.nih.gov/medlineplus/headandbrainmalformations.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 cleft palate. 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:

- **Cleft Palate and Hearing Loss**

  Source: Chapel Hill, NC: Cleft Palate Foundation. 2002. [6 p.].

  Contact: Available from Cleft Palate Foundation. 104 South Estes Drive, Suite 204, Chapel Hill, NC 27514. (800) 24-CLEFT or (800) 242-5338 or (919) 933-9044. Fax (919) 933-9604. E-mail: cleftline@aol.com. Website: www.cleftline.org. PRICE: Single copy free.

  Summary: Hearing loss is the most common birth defect found in newborns, even in babies without cleft lip or palate. Many hospitals now screen newborns' hearing before they even leave the hospital. This brochure reviews the problems of cleft palate and hearing loss occurring together in children. The brochure discusses how young children's hearing and ears are evaluated, the different types of hearing loss, cleft palate and middle ear disease, why children with cleft palate are more likely to have ear infections, ear infections and hearing, the use of tubes to treat middle ear problems, speech and language development, common speech disorders related to persistent ear

infections, common language disorders related to persistent ear infections, and speech and language treatment. The brochure concludes by reiterating the importance of working closely with a cleft palate team of health care providers. Contact information for the Cleft Palate Foundation (www.cleftline.org) is provided. 3 figures.

- **Cleft lip and cleft palate: The first four years. (Rev. ed.)**

  Source: Chapel Hill, NC: Cleft Palate Foundation. 1998. 24 pp.

  Contact: Available from Cleft Palate Foundation, 1829 East Franklin Street, Suite 1022, Chapel Hill, NC 27514. Telephone: (919) 933-9044.

  Summary: The purpose of this booklet is to provide answers for the questions of parents about what can be done to help their baby with a cleft and lessen parental concerns about the future. The information has been prepared by health care professionals who are members of the American Cleft Palate - Craniofacial Association and by lay persons who are members of parent-patient support groups. Much of the information in this booklet is based on interactions with parents. The information in the booklet will help parents know how to care for their their baby and is presented in the general order in which parents may need to cope with various situations. A glossary at the end of the booklet defines certain words parents may read or hear. Words in the glossary are bolded when they first appear in the booklet.

- **Nursing Your Baby with a Cleft Palate or Cleft Lip**

  Source: Waco, TX: Childbirth Graphics, Health EDCO. 1996. 16 p.

  Contact: Available from Childbirth Graphics. Health EDCO, P.O. Box 21207, Waco, TX 76702-1207. (800) 299-3366 or (817) 776-6461. Fax (888) 977-7653. PRICE: Single copy free; bulk rates available.

  Summary: This booklet helps mothers of infants with cleft palate or cleft lip successfully breastfeed their babies. The brochure briefly reviews the benefits of breastfeeding, including fewer infections, essential parent-infant interaction and closeness, better face and mouth development, and extra protection after oral surgery. The brochure then provides detailed suggestions for breastfeeding a baby with a cleft lip or cleft palate. Other topics include dealing with a palatal obturator, helping the infant to nurse adequately, finding different positions to support nursing, using chin support for the baby, burping, breastfeeding after oral surgery, establishing the length of feedings, stimulating the milk supplies, supplementing the breastfeeding with a pacifier feeding technique, and the importance of taking good care of the mother, both physically and psychologically. The brochure is illustrated with numerous black and white photographs depicting babies with clefts in various nursing positions. The brochure concludes with information about the Cleft Palate Foundation and with suggestions for finding other support groups, including the La Leche League.

- **Cleft Lip and Cleft Palate: Information for the Teenager Born with a Cleft**

  Source: Chapel Hill, NC: Cleft Palate Foundation. 1997. 14 p.

  Contact: Available from Cleft Palate Foundation. 104 South Estes Drive, Suite 204, Chapel Hill, NC 27514. (800) 242-5338. Fax (919) 933-9604. E-mail: cleftline@aol.com. Website: www.cleft.com. PRICE: Single copy free.

  Summary: This booklet provides information about concerns that teenagers born with a cleft lip or a cleft palate may have. The booklet notes that, by the teenage years, most

children will have undergone primary surgeries repairing the cleft, but may still have some questions about additional treatment or other issues. The booklet includes eight chapters that cover the development and genetics of cleft lip and palate, surgery and surgical techniques, additional surgery, otolaryngology and the role of the otolaryngologist, orthodontics (braces) and oral hygiene, prosthodontics, speech language therapy, and social functioning. A final section briefly describes a number of programs specifically designed for teenagers and young adults with clefts. The brochure concludes that, generally speaking, teenagers with clefts have the same chance to be physically and emotionally healthy as do their noncleft peers.

- **Choosing a Cleft Palate or Craniofacial Team**

  Source: Chapel Hill, NC: Cleft Palate Foundation. 2000. 2 p.

  Contact: Available from Cleft Palate Foundation. 104 South Estes Drive, Suite 204, Chapel Hill, NC 27514. (800) 242-5338. Fax (919) 933-9604. E-mail: cleftline@aol.com. Website: www.cleft.com. PRICE: Single copy free.

  Summary: This fact sheet provides information for the parents of a child with cleft lip or palate or other craniofacial anomalies. The fact sheet offers suggestions for choosing a cleft palate or craniofacial team, the health professionals who care for these children. The author notes that these children frequently require a number of different types of services which need to be provided in a coordinated manner over a period of years. The principal role of the interdisciplinary team is to provide integrated case management for the child, assure quality and continuity of care, and render long term follow-up. The fact sheet outlines the different specialists who actually participate on the craniofacial team. Other topics covered are qualifications of the individual members of the team, experience of the team, location of the team, affiliation of the team and its members, and communication with the team. The fact sheet concludes with the address and telephone number of the Cleft Palate Foundation. 1 reference.

- **Cleft Palate: Seeing What is Beautiful**

  Source: in DeFeo, A.B., ed. Parent Articles 2. San Antonio, TX: Communication Skill Builders. 1995. p. 175-177.

  Contact: Available from Communication Skill Builders. Customer Service, 555 Academic Court, San Antonio, TX 78204-2498. (800) 211-8378; Fax (800) 232-1223. PRICE: $55.00 plus shipping and handling. Order Number 3073-CS5.

  Summary: This fact sheet, from a communication skills book for parents, discusses the emotions and psychological factors that may affect the parents of children with clefts. Topics include the author's own story and her emotions at first seeing her babies with clefts, handling the reactions of others, psychosocial concerns as the child develops, medical issues, coping with the long-term nature of surgery and rehabilitation, the role of speech-language therapy, and the need for parents to build a support network. The author encourages parents to educate themselves, to draw on other parents for support, and to act as their child's advocate.

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:

- **Cleft Palate Foundation Publications**

  Summary: Fact sheets from the cleft platate foundation.

  Source: American Cleft Palate-Craniofacial Association Cleft Palate Foundation

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7591

- **Information for Parents: Cleft Lip and Cleft Palate**

  Summary: On this page you'll find information on caring for your cleft-affected newborn, basics on doctors, what to tell siblings, taking pictures, stress reduction, and starting your own support groups.

  Source: Wide Smiles

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7673

- **SMILES**

  Summary: A web site designed to meet the needs of parents of children born with cleft lip, cleft palate and craniofacial deformities.

  Source: Commercial Entity--Follow the Resource URL for More Information

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6079

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 cleft palate. 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**

Associations and Cleft Palate

The following is a list of associations that provide information on and resources relating to cleft palate:

- **Cleft Palate Foundation**

  Telephone: (919) 933-9044 Toll-free: (800) 242-5338

  Fax: (919) 933-9604

  Email: info@cleftline.org

  Web Site: http://www.cleftline.org

  Background: The **Cleft Palate** Foundation was founded by its parent organization, the American **Cleft Palate** Craniofacial Association, as the public service arm of this professional organization. The purpose of the Foundation is to educate and assist the public concerning cleft lip, **cleft palate,** and other related craniofacial anomalies. The Foundation also seeks to encourage medical research in the field of craniofacial anomalies. The Foundation operates the CLEFTLINE, a toll-free service that provides information and referrals for parents with newborns who have cleft lip and/or **cleft palate** and for others affected by these abnormalities. The Foundation also offers free brochures and fact sheets on various aspects of these birth defects.

  Relevant area(s) of interest: Cleft Palate

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to cleft palate. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with cleft palate.

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 cleft palate. 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 "cleft palate" (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 "cleft palate". 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 "cleft palate" (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 "cleft palate" (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.[21]

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

[21] 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)[22]:

- **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/**

[22] 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**).

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**

CLEFT PALATE DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

Abdomen: That portion of the body that lies between the thorax and the pelvis. [NIH]

Abdominal: Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Aberrant: Wandering or deviating from the usual or normal course. [EU]

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]

Accommodation: Adjustment, especially that of the eye for various distances. [EU]

Acetaminophen: Analgesic antipyretic derivative of acetanilide. It has weak anti-inflammatory properties and is used as a common analgesic, but may cause liver, blood cell, and kidney damage. [NIH]

Acetylgalactosamine: The N-acetyl derivative of galactosamine. [NIH]

Acetylglucosamine: The N-acetyl derivative of glucosamine. [NIH]

Acoustic: Having to do with sound or hearing. [NIH]

Actin: Essential component of the cell skeleton. [NIH]

Adaptability: Ability to develop some form of tolerance to conditions extremely different from those under which a living organism evolved. [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]

Adjustment: The dynamic process wherein the thoughts, feelings, behavior, and biophysiological mechanisms of the individual continually change to adjust to the environment. [NIH]

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 Cortex: The outer layer of the adrenal gland. It secretes mineralocorticoids, androgens, and glucocorticoids. [NIH]

Adverse Effect: An unwanted side effect of treatment. [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]

Agenesis: Lack of complete or normal development; congenital absence of an organ or part. [NIH]

Airway: A device for securing unobstructed passage of air into and out of the lungs during general anesthesia. [NIH]

Airway Resistance: Physiologically, the opposition to flow of air caused by the forces of friction. As a part of pulmonary function testing, it is the ratio of driving pressure to the rate of air flow. [NIH]

Alexia: The inability to recognize or comprehend written or printed words. [NIH]

Alfalfa: A deep-rooted European leguminous plant (Medicago sativa) widely grown for hay and forage. [NIH]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [NIH]

Alkaline: Having the reactions of an alkali. [EU]

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on homologous chromosomes, and governing the same biochemical and developmental process. [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]

Alveoli: Tiny air sacs at the end of the bronchioles in the lungs. [NIH]

Ameliorating: A changeable condition which prevents the consequence of a failure or accident from becoming as bad as it otherwise would. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amniotic Fluid: Amniotic cavity fluid which is produced by the amnion and fetal lungs and kidneys. [NIH]

Anaemia: A reduction below normal in the number of erythrocytes per cu. mm., in the quantity of haemoglobin, or in the volume of packed red cells per 100 ml. of blood which occurs when the equilibrium between blood loss (through bleeding or destruction) and blood production is disturbed. [EU]

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]

Anal: Having to do with the anus, which is the posterior opening of the large bowel. [NIH]

Analgesic: An agent that alleviates pain without causing loss of consciousness. [EU]

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]

Androgens: A class of sex hormones associated with the development and maintenance of the secondary male sex characteristics, sperm induction, and sexual differentiation. In addition to increasing virility and libido, they also increase nitrogen and water retention and stimulate skeletal growth. [NIH]

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]

Aneuploidy: The chromosomal constitution of cells which deviate from the normal by the addition or subtraction of chromosomes or chromosome pairs. In a normally diploid cell the loss of a chromosome pair is termed nullisomy (symbol: 2N-2), the loss of a single chromosome is monosomy (symbol: 2N-1), the addition of a chromosome pair is tetrasomy (symbol: 2N+2), the addition of a single chromosome is trisomy (symbol: 2N+1). [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]

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]

Anomalies: Birth defects; abnormalities. [NIH]

Antiallergic: Counteracting allergy or allergic conditions. [EU]

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]

Anticonvulsant: An agent that prevents or relieves convulsions. [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-inflammatory: Having to do with reducing inflammation. [NIH]

Anti-Inflammatory Agents: Substances that reduce or suppress inflammation. [NIH]

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]

Antipyretic: An agent that relieves or reduces fever. Called also antifebrile, antithermic and febrifuge. [EU]

Anus: The opening of the rectum to the outside of the body. [NIH]

Anxiety: Persistent feeling of dread, apprehension, and impending disaster. [NIH]

Aorta: The main trunk of the systemic arteries. [NIH]

Aplasia: Lack of development of an organ or tissue, or of the cellular products from an organ or tissue. [EU]

Apnea: A transient absence of spontaneous respiration. [NIH]

Aponeurosis: Tendinous expansion consisting of a fibrous or membranous sheath which serves as a fascia to enclose or bind a group of muscles. [NIH]

Apoptosis: One of the two mechanisms by which cell death occurs (the other being the pathological process of necrosis). Apoptosis is the mechanism responsible for the physiological deletion of cells and appears to be intrinsically programmed. It is characterized by distinctive morphologic changes in the nucleus and cytoplasm, chromatin cleavage at regularly spaced sites, and the endonucleolytic cleavage of genomic DNA (DNA fragmentation) at internucleosomal sites. This mode of cell death serves as a balance to mitosis in regulating the size of animal tissues and in mediating pathologic processes associated with tumor growth. [NIH]

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]

Aromatic: Having a spicy odour. [EU]

Arrhythmia: Any variation from the normal rhythm or rate of the heart beat. [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]

Arteriosclerosis: Thickening and loss of elasticity of arterial walls. Atherosclerosis is the most common form of arteriosclerosis and involves lipid deposition and thickening of the intimal cell layers within arteries. Additional forms of arteriosclerosis involve calcification of the media of muscular arteries (Monkeberg medial calcific sclerosis) and thickening of the walls of small arteries or arterioles due to cell proliferation or hyaline deposition (arteriolosclerosis). [NIH]

Arteriovenous: Both arterial and venous; pertaining to or affecting an artery and a vein. [EU]

Articulation: The relationship of two bodies by means of a moveable joint. [NIH]

Articulation Disorders: Disorders of the quality of speech characterized by the substitution, omission, distortion, and addition of phonemes. [NIH]

Aseptic: Free from infection or septic material; sterile. [EU]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Ataxia: Impairment of the ability to perform smoothly coordinated voluntary movements. This condition may affect the limbs, trunk, eyes, pharnyx, larnyx, and other structures. Ataxia may result from impaired sensory or motor function. Sensory ataxia may result from posterior column injury or peripheral nerve diseases. Motor ataxia may be associated with cerebellar diseases; cerebral cortex diseases; thalamic diseases; basal ganglia diseases; injury to the red nucleus; and other conditions. [NIH]

Atrium: A chamber; used in anatomical nomenclature to designate a chamber affording entrance to another structure or organ. Usually used alone to designate an atrium of the heart. [EU]

Atypical: Irregular; not conformable to the type; in microbiology, applied specifically to strains of unusual type. [EU]

Auditory: Pertaining to the sense of hearing. [EU]

Autopsy: Postmortem examination of the body. [NIH]

Autosuggestion: Suggestion coming from the subject himself. [NIH]

Avian: A plasmodial infection in birds. [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 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]

Bacterium: Microscopic organism which may have a spherical, rod-like, or spiral unicellular or non-cellular body. Bacteria usually reproduce through asexual processes. [NIH]

Base: In chemistry, the nonacid part of a salt; a substance that combines with acids to form salts; a substance that dissociates to give hydroxide ions in aqueous solutions; a substance whose molecule or ion can combine with a proton (hydrogen ion); a substance capable of donating a pair of electrons (to an acid) for the formation of a coordinate covalent bond. [EU]

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]

Basilar Artery: The artery formed by the union of the right and left vertebral arteries; it runs from the lower to the upper border of the pons, where it bifurcates into the two posterior cerebral arteries. [NIH]

Bereavement: Refers to the whole process of grieving and mourning and is associated with a deep sense of loss and sadness. [NIH]

Bifida: A defect in development of the vertebral column in which there is a central deficiency of the vertebral lamina. [NIH]

Bilateral: Affecting both the right and left side of body. [NIH]

Bile: An emulsifying agent produced in the liver and secreted into the duodenum. Its composition includes bile acids and salts, cholesterol, and electrolytes. It aids digestion of

fats in the duodenum. [NIH]

Bile Acids: Acids made by the liver that work with bile to break down fats. [NIH]

Binding Sites: The reactive parts of a macromolecule that directly participate in its specific combination with another molecule. [NIH]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

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]

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]

Biotin: Hexahydro-2-oxo-1H-thieno(3,4-d)imidazole-4-pentanoic acid. Growth factor present in minute amounts in every living cell. It occurs mainly bound to proteins or polypeptides and is abundant in liver, kidney, pancreas, yeast, and milk.The biotin content of cancerous tissue is higher than that of normal tissue. [NIH]

Birth Certificates: Official certifications by a physician recording the individual's birth date, place of birth, parentage and other required identifying data which are filed with the local registrar of vital statistics. [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 Platelets: Non-nucleated disk-shaped cells formed in the megakaryocyte and found in the blood of all mammals. They are mainly involved in blood coagulation. [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]

Body Fluids: Liquid components of living organisms. [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 Regeneration: Renewal or repair of lost bone tissue. It excludes bony callus formed after bone fracture but not yet replaced by hard bone. [NIH]

Bowel: The long tube-shaped organ in the abdomen that completes the process of digestion. There is both a small and a large bowel. Also called the intestine. [NIH]

Bowel Movement: Body wastes passed through the rectum and anus. [NIH]

Brachial: All the nerves from the arm are ripped from the spinal cord. [NIH]

Brain Neoplasms: Neoplasms of the intracranial components of the central nervous system,

including the cerebral hemispheres, basal ganglia, hypothalamus, thalamus, brain stem, and cerebellum. Brain neoplasms are subdivided into primary (originating from brain tissue) and secondary (i.e., metastatic) forms. Primary neoplasms are subdivided into benign and malignant forms. In general, brain tumors may also be classified by age of onset, histologic type, or presenting location in the brain. [NIH]

Branch: Most commonly used for branches of nerves, but applied also to other structures. [NIH]

Buccal: Pertaining to or directed toward the cheek. In dental anatomy, used to refer to the buccal surface of a tooth. [EU]

Buccal mucosa: The inner lining of the cheeks and lips. [NIH]

Buccopharyngeal: Pertaining to the mouth and pharynx. [EU]

Bypass: A surgical procedure in which the doctor creates a new pathway for the flow of body fluids. [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]

Callus: A callosity or hard, thick skin; the bone-like reparative substance that is formed round the edges and fragments of broken bone. [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]

Carcinogen: Any substance that causes cancer. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Cardiac: Having to do with the heart. [NIH]

Cardiology: The study of the heart, its physiology, and its functions. [NIH]

Cardiovascular: Having to do with the heart and blood vessels. [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-Control Studies: Studies which start with the identification of persons with a disease of interest and a control (comparison, referent) group without the disease. The relationship of an attribute to the disease is examined by comparing diseased and non-diseased persons with regard to the frequency or levels of the attribute in each group. [NIH]

Catabolism: Any destructive metabolic process by which organisms convert substances into excreted compounds. [EU]

Caudal: Denoting a position more toward the cauda, or tail, than some specified point of reference; same as inferior, in human anatomy. [EU]

Causal: Pertaining to a cause; directed against a cause. [EU]

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 Adhesion: Adherence of cells to surfaces or to other 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 Death: The termination of the cell's ability to carry out vital functions such as metabolism, growth, reproduction, responsiveness, and adaptability. [NIH]

Cell Differentiation: Progressive restriction of the developmental potential and increasing specialization of function which takes place during the development of the embryo and leads to the formation of specialized cells, tissues, and organs. [NIH]

Cell Division: The fission of a cell. [NIH]

Cell Lineage: The developmental history of cells as traced from the first division of the original cell or cells in the embryo. [NIH]

Cell membrane: Cell membrane = plasma membrane. The structure enveloping a cell, enclosing the cytoplasm, and forming a selective permeability barrier; it consists of lipids, proteins, and some carbohydrates, the lipids thought to form a bilayer in which integral proteins are embedded to varying degrees. [EU]

Cell Movement: The movement of cells from one location to another. [NIH]

Cell proliferation: An increase in the number of cells as a result of cell growth and cell division. [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]

Central Nervous System: The main information-processing organs of the nervous system, consisting of the brain, spinal cord, and meninges. [NIH]

Central Nervous System Infections: Pathogenic infections of the brain, spinal cord, and meninges. DNA virus infections; RNA virus infections; bacterial infections; mycoplasma infections; Spirochaetales infections; fungal infections; protozoan infections; helminthiasis; and prion diseases may involve the central nervous system as a primary or secondary process. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

Cerebellum: Part of the metencephalon that lies in the posterior cranial fossa behind the brain stem. It is concerned with the coordination of movement. [NIH]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cerebral Arteries: The arteries supplying the cerebral cortex. [NIH]

Cerebral Infarction: The formation of an area of necrosis in the cerebrum caused by an insufficiency of arterial or venous blood flow. Infarcts of the cerebrum are generally classified by hemisphere (i.e., left vs. right), lobe (e.g., frontal lobe infarction), arterial distribution (e.g., infarction, anterior cerebral artery), and etiology (e.g., embolic infarction). [NIH]

Cerebrospinal: Pertaining to the brain and spinal cord. [EU]

Cerebrospinal fluid: CSF. The fluid flowing around the brain and spinal cord. Cerebrospinal fluid is produced in the ventricles in the brain. [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]

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]

Choanal Atresia: Congenital bony or membranous occlusion of one or both choanae, due to failure of the embryonic bucconasal membrane to rupture. [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]

Chromatin: The material of chromosomes. It is a complex of DNA, histones, and nonhistone proteins (chromosomal proteins, non-histone) found within the nucleus of a cell. [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]

Chromosome Abnormalities: Defects in the structure or number of chromosomes resulting in structural aberrations or manifesting as disease. [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [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]

Cleft Palate: Congenital fissure of the soft and/or hard palate, due to faulty fusion. [NIH]

Clinical Medicine: The study and practice of medicine by direct examination of the patient. [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]

Cochlea: The part of the internal ear that is concerned with hearing. It forms the anterior part of the labyrinth, is conical, and is placed almost horizontally anterior to the vestibule. [NIH]

Cochlear: Of or pertaining to the cochlea. [EU]

Cochlear Diseases: Diseases of the cochlea, the part of the inner ear that is concerned with hearing. [NIH]

Cochlear Implants: Electronic devices implanted beneath the skin with electrodes to the cochlear nerve to create sound sensation in persons with sensorineural deafness. [NIH]

Cochlear Nerve: The cochlear part of the 8th cranial nerve (vestibulocochlear nerve). The cochlear nerve fibers originate from neurons of the spiral ganglion and project peripherally

to cochlear hair cells and centrally to the cochlear nuclei (cochlear nucleus) of the brain stem. They mediate the sense of hearing. [NIH]

Cofactor: A substance, microorganism or environmental factor that activates or enhances the action of another entity such as a disease-causing agent. [NIH]

Cognition: Intellectual or mental process whereby an organism becomes aware of or obtains knowledge. [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]

Colitis: Inflammation of the colon. [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]

Collapse: 1. A state of extreme prostration and depression, with failure of circulation. 2. Abnormal falling in of the walls of any part of organ. [EU]

Colloidal: Of the nature of a colloid. [EU]

Coloboma: Congenital anomaly in which some of the structures of the eye are absent due to incomplete fusion of the fetal intraocular fissure during gestation. [NIH]

Communication Disorders: Disorders of verbal and nonverbal communication caused by receptive or expressive language disorders, cognitive dysfunction (e.g., mental retardation), psychiatric conditions, and hearing disorders. [NIH]

Competency: The capacity of the bacterium to take up DNA from its surroundings. [NIH]

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]

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]

Cone: One of the special retinal receptor elements which are presumed to be primarily concerned with perception of light and color stimuli when the eye is adapted to light. [NIH]

Confounding: Extraneous variables resulting in outcome effects that obscure or exaggerate the "true" effect of an intervention. [NIH]

Congenita: Displacement, subluxation, or malposition of the crystalline lens. [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]

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 Cells: A group of cells that includes fibroblasts, cartilage cells, adipocytes, smooth muscle cells, and bone cells. [NIH]

Consciousness: Sense of awareness of self and of the environment. [NIH]

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]

Consumption: Pulmonary tuberculosis. [NIH]

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]

Controlled study: An experiment or clinical trial that includes a comparison (control) group. [NIH]

Cornea: The transparent part of the eye that covers the iris and the pupil and allows light to enter the inside. [NIH]

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 Thrombosis: Presence of a thrombus in a coronary artery, often causing a myocardial infarction. [NIH]

Corpus: The body of the uterus. [NIH]

Corpus Callosum: Broad plate of dense myelinated fibers that reciprocally interconnect regions of the cortex in all lobes with corresponding regions of the opposite hemisphere. The corpus callosum is located deep in the longitudinal fissure. [NIH]

Cortex: The outer layer of an organ or other body structure, as distinguished from the internal substance. [EU]

Cortices: The outer layer of an organ; used especially of the cerebrum and cerebellum. [NIH]

Corticosteroid: Any of the steroids elaborated by the adrenal cortex (excluding the sex hormones of adrenal origin) in response to the release of corticotrophin (adrenocorticotropic hormone) by the pituitary gland, to any of the synthetic equivalents of these steroids, or to angiotensin II. They are divided, according to their predominant biological activity, into three major groups: glucocorticoids, chiefly influencing carbohydrate, fat, and protein metabolism; mineralocorticoids, affecting the regulation of electrolyte and water balance; and C19 androgens. Some corticosteroids exhibit both types of activity in varying degrees, and others exert only one type of effect. The corticosteroids are used clinically for hormonal replacement therapy, for suppression of ACTH secretion by the anterior pituitary, as antineoplastic, antiallergic, and anti-inflammatory agents, and to suppress the immune response. Called also adrenocortical hormone and corticoid. [EU]

Cortisone: A natural steroid hormone produced in the adrenal gland. It can also be made in the laboratory. Cortisone reduces swelling and can suppress immune responses. [NIH]

Cranial: Pertaining to the cranium, or to the anterior (in animals) or superior (in humans) end of the body. [EU]

Craniocerebral Trauma: Traumatic injuries involving the cranium and intracranial structures (i.e., brain; cranial nerves; meninges; and other structures). Injuries may be classified by whether or not the skull is penetrated (i.e., penetrating vs. nonpenetrating) or whether there is an associated hemorrhage. [NIH]

Craniofacial Abnormalities: Congenital structural deformities, malformations, or other abnormalities of the cranium and facial bones. [NIH]

Crossing-over: The exchange of corresponding segments between chromatids of homologous chromosomes during meiosia, forming a chiasma. [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]

Cryptorchidism: A condition in which one or both testicles fail to move from the abdomen, where they develop before birth, into the scrotum. Cryptorchidism may increase the risk for development of testicular cancer. Also called undescended testicles. [NIH]

Cultured cells: Animal or human cells that are grown in the laboratory. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Cyclic: Pertaining to or occurring in a cycle or cycles; the term is applied to chemical compounds that contain a ring of atoms in the nucleus. [EU]

Cyclin: Molecule that regulates the cell cycle. [NIH]

Cyclooxygenase Inhibitors: Compounds or agents that combine with cyclooxygenase (prostaglandin-endoperoxide synthase) and thereby prevent its substrate-enzyme

combination with arachidonic acid and the formation of eicosanoids, prostaglandins, and thromboxanes. [NIH]

Cyst: A sac or capsule filled with fluid. [NIH]

Cytogenetics: A branch of genetics which deals with the cytological and molecular behavior of genes and chromosomes during cell division. [NIH]

Cytokine: Small but highly potent protein that modulates the activity of many cell types, including T and B cells. [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]

Cytoskeleton: The network of filaments, tubules, and interconnecting filamentous bridges which give shape, structure, and organization to the cytoplasm. [NIH]

Cytotoxic: Cell-killing. [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]

Databases, Bibliographic: Extensive collections, reputedly complete, of references and citations to books, articles, publications, etc., generally on a single subject or specialized subject area. Databases can operate through automated files, libraries, or computer disks. The concept should be differentiated from factual databases which is used for collections of data and facts apart from bibliographic references to them. [NIH]

De novo: In cancer, the first occurrence of cancer in the body. [NIH]

Decidua: The epithelial lining of the endometrium that is formed before the fertilized ovum reaches the uterus. The fertilized ovum embeds in the decidua. If the ovum is not fertilized, the decidua is shed during menstruation. [NIH]

Decision Making: The process of making a selective intellectual judgment when presented with several complex alternatives consisting of several variables, and usually defining a course of action or an idea. [NIH]

Defense Mechanisms: Unconscious process used by an individual or a group of individuals in order to cope with impulses, feelings or ideas which are not acceptable at their conscious level; various types include reaction formation, projection and self reversal. [NIH]

Deletion: A genetic rearrangement through loss of segments of DNA (chromosomes), bringing sequences, which are normally separated, into close proximity. [NIH]

Dementia: An acquired organic mental disorder with loss of intellectual abilities of sufficient severity to interfere with social or occupational functioning. The dysfunction is multifaceted and involves memory, behavior, personality, judgment, attention, spatial relations, language, abstract thought, and other executive functions. The intellectual decline is usually progressive, and initially spares the level of consciousness. [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 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 implant: A small metal pin placed inside the jawbone to mimic the root of a tooth. Dental implants can be used to help anchor a false tooth or teeth, or a crown or bridge. [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]

Dentition, Primary: The teeth first in order or time of development that will be replaced by permanent dentition upon their loss. [NIH]

Depigmentation: Removal or loss of pigment, especially melanin. [EU]

Depolarization: The process or act of neutralizing polarity. In neurophysiology, the reversal of the resting potential in excitable cell membranes when stimulated, i.e., the tendency of the cell membrane potential to become positive with respect to the potential outside the cell. [EU]

Deprivation: Loss or absence of parts, organs, powers, or things that are needed. [EU]

Dermal: Pertaining to or coming from the skin. [NIH]

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]

Dexterity: Ability to move the hands easily and skillfully. [NIH]

Diagnostic procedure: A method used to identify a disease. [NIH]

Digestion: The process of breakdown of food for metabolism and use by the body. [NIH]

Digestive system: The organs that take in food and turn it into products that the body can use to stay healthy. Waste products the body cannot use leave the body through bowel movements. The digestive system includes the salivary glands, mouth, esophagus, stomach, liver, pancreas, gallbladder, small and large intestines, and rectum. [NIH]

Dihydrotestosterone: Anabolic agent. [NIH]

Dilation: A process by which the pupil is temporarily enlarged with special eye drops (mydriatic); allows the eye care specialist to better view the inside of the eye. [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]

Disinfectant: An agent that disinfects; applied particularly to agents used on inanimate objects. [EU]

Dissection: Cutting up of an organism for study. [NIH]

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]

Dizziness: An imprecise term which may refer to a sense of spatial disorientation, motion of the environment, or lightheadedness. [NIH]

Dorsal: 1. Pertaining to the back or to any dorsum. 2. Denoting a position more toward the back surface than some other object of reference; same as posterior in human anatomy; superior in the anatomy of quadrupeds. [EU]

Dose-dependent: Refers to the effects of treatment with a drug. If the effects change when the dose of the drug is changed, the effects are said to be dose dependent. [NIH]

Drug Interactions: The action of a drug that may affect the activity, metabolism, or toxicity of another drug. [NIH]

Duct: A tube through which body fluids pass. [NIH]

Dyslexia: Partial alexia in which letters but not words may be read, or in which words may be read but not understood. [NIH]

Dysplasia: Cells that look abnormal under a microscope but are not cancer. [NIH]

Dystonia: Disordered tonicity of muscle. [EU]

Dystrophic: Pertaining to toxic habitats low in nutrients. [NIH]

Dystrophy: Any disorder arising from defective or faulty nutrition, especially the muscular dystrophies. [EU]

Ectoderm: The outer of the three germ layers of the embryo. [NIH]

Ectodermal Dysplasia: A group of hereditary disorders involving tissues and structures derived from the embryonic ectoderm. They are characterized by the presence of abnormalities at birth and involvement of both the epidermis and skin appendages. They are generally nonprogressive and diffuse. Various forms exist, including anhidrotic and hidrotic dysplasias, focal dermal hypoplasia, and aplasia cutis congenita. [NIH]

Ectopic: Pertaining to or characterized by ectopia. [EU]

Edema: Excessive amount of watery fluid accumulated in the intercellular spaces, most commonly present in subcutaneous tissue. [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]

Effusion: The escape of fluid into a part or tissue, as an exudation or a transudation. [EU]

Eicosanoids: A class of oxygenated, endogenous, unsaturated fatty acids derived from arachidonic acid. They include prostaglandins, leukotrienes, thromboxanes, and hydroxyeicosatetraenoic acid compounds (HETE). They are hormone-like substances that act near the site of synthesis without altering functions throughout the body. [NIH]

Elastin: The protein that gives flexibility to tissues. [NIH]

Elective: Subject to the choice or decision of the patient or physician; applied to procedures that are advantageous to the patient but not urgent. [EU]

Electrolyte: A substance that dissociates into ions when fused or in solution, and thus becomes capable of conducting electricity; an ionic solute. [EU]

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]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

Embryogenesis: The process of embryo or embryoid formation, whether by sexual (zygotic) or asexual means. In asexual embryogenesis embryoids arise directly from the explant or on intermediary callus tissue. In some cases they arise from individual cells (somatic cell embryoge). [NIH]

Empirical: A treatment based on an assumed diagnosis, prior to receiving confirmatory laboratory test results. [NIH]

Enamel: A very hard whitish substance which covers the dentine of the anatomical crown of a tooth. [NIH]

Encephalocele: Cerebral tissue herniation through a congenital or acquired defect in the skull. The majority of congenital encephaloceles occur in the occipital or frontal regions. Clinical features include a protuberant mass that may be pulsatile. The quantity and location of protruding neural tissue determines the type and degree of neurologic deficit. Visual

defects, psychomotor developmental delay, and persistent motor deficits frequently occur. [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]

Endocrine Glands: Ductless glands that secrete substances which are released directly into the circulation and which influence metabolism and other body functions. [NIH]

Endoscope: A thin, lighted tube used to look at tissues inside the body. [NIH]

Enteric Nervous System: The entire nerve apparatus composed of the brain, spinal cord, nerves and ganglia. [NIH]

Environmental Exposure: The exposure to potentially harmful chemical, physical, or biological agents in the environment or to environmental factors that may include ionizing radiation, pathogenic organisms, or toxic chemicals. [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]

Eosinophilia: Abnormal increase in eosinophils in the blood, tissues or organs. [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]

Epidemic: Occurring suddenly in numbers clearly in excess of normal expectancy; said especially of infectious diseases but applied also to any disease, injury, or other health-related event occurring in such outbreaks. [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]

Epidermolysis Bullosa: Group of genetically determined disorders characterized by the blistering of skin and mucosae. There are four major forms: acquired, simple, junctional, and dystrophic. Each of the latter three has several varieties. [NIH]

Epinephrine: The active sympathomimetic hormone from the adrenal medulla in most species. It stimulates both the alpha- and beta- adrenergic systems, causes systemic vasoconstriction and gastrointestinal relaxation, stimulates the heart, and dilates bronchi and cerebral vessels. It is used in asthma and cardiac failure and to delay absorption of local anesthetics. [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]

Epithelium: One or more layers of epithelial cells, supported by the basal lamina, which covers the inner or outer surfaces of the body. [NIH]

Erythrocytes: Red blood cells. Mature erythrocytes are non-nucleated, biconcave disks containing hemoglobin whose function is to transport oxygen. [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]

Eustachian tube: The middle ear cavity is in communication with the back of the nose through the Eustachian tube, which is normally closed, but opens on swallowing, in order to maintain equal air pressure. [NIH]

Excitatory: When cortical neurons are excited, their output increases and each new input they receive while they are still excited raises their output markedly. [NIH]

Exons: Coding regions of messenger RNA included in the genetic transcript which survive the processing of RNA in cell nuclei to become part of a spliced messenger of structural RNA in the cytoplasm. They include joining and diversity exons of immunoglobulin genes. [NIH]

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]

Expiratory: The volume of air which leaves the breathing organs in each expiration. [NIH]

Extender: 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. [NIH]

Extensor: A muscle whose contraction tends to straighten a limb; the antagonist of a flexor. [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]

Facial: Of or pertaining to the face. [EU]

Family Health: The health status of the family as a unit including the impact of the health of one member of the family on the family as a unit and on individual family members; also, the impact of family organization or disorganization on the health status of its members. [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]

Fatty acids: A major component of fats that are used by the body for energy and tissue development. [NIH]

Fetal Development: Morphologic and physiologic growth and development of the mammalian embryo or fetus. [NIH]

Fetus: The developing offspring from 7 to 8 weeks after conception until birth. [NIH]

Fibroblasts: Connective tissue cells which secrete an extracellular matrix rich in collagen and other macromolecules. [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]

Fistula: Abnormal communication most commonly seen between two internal organs, or between an internal organ and the surface of the body. [NIH]

Folate: A B-complex vitamin that is being studied as a cancer prevention agent. Also called folic acid. [NIH]

Fold: A plication or doubling of various parts of the body. [NIH]

Folic Acid: N-(4-(((2-Amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl)amino)benzoyl)-L-glutamic acid. A member of the vitamin B family that stimulates the hematopoietic system. It is present in the liver and kidney and is found in mushrooms, spinach, yeast, green leaves, and grasses. Folic acid is used in the treatment and prevention of folate deficiencies and megaloblastic anemia. [NIH]

Follicles: Shafts through which hair grows. [NIH]

Foramen: A natural hole of perforation, especially one in a bone. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Fossa: A cavity, depression, or pit. [NIH]

Friction: Surface resistance to the relative motion of one body against the rubbing, sliding, rolling, or flowing of another with which it is in contact. [NIH]

Gallbladder: The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Ganglion: 1. A knot, or knotlike mass. 2. A general term for a group of nerve cell bodies located outside the central nervous system; occasionally applied to certain nuclear groups within the brain or spinal cord, e.g. basal ganglia. 3. A benign cystic tumour occurring on a aponeurosis or tendon, as in the wrist or dorsum of the foot; it consists of a thin fibrous capsule enclosing a clear mucinous fluid. [EU]

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]

Gas exchange: Primary function of the lungs; transfer of oxygen from inhaled air into the blood and of carbon dioxide from the blood into the lungs. [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gastritis: Inflammation of the stomach. [EU]

Gastroesophageal Reflux: Reflux of gastric juice and/or duodenal contents (bile acids, pancreatic juice) into the distal esophagus, commonly due to incompetence of the lower esophageal sphincter. Gastric regurgitation is an extension of this process with entry of fluid

into the pharynx or mouth. [NIH]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [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]

Genetic Counseling: Advising families of the risks involved pertaining to birth defects, in order that they may make an informed decision on current or future pregnancies. [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]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genital: Pertaining to the genitalia. [EU]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Gestation: The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

Gestational: Psychosis attributable to or occurring during pregnancy. [NIH]

Gestational Age: Age of the conceptus. In humans, this may be assessed by medical history, physical examination, early immunologic pregnancy tests, radiography, ultrasonography, and amniotic fluid analysis. [NIH]

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]

Glossopalatine: A root of the facial nerve arising from the sensory nucleus, lateral and posterior to the motor root, containing parasympathetic fibers coursing to the lacrimal gland via the great superficial petrosal nerve which synapses in the sphenopalatine ganglion. [NIH]

Glucocorticoids: A group of corticosteroids that affect carbohydrate metabolism (gluconeogenesis, liver glycogen deposition, elevation of blood sugar), inhibit corticotropin secretion, and possess pronounced anti-inflammatory activity. They also play a role in fat and protein metabolism, maintenance of arterial blood pressure, alteration of the connective tissue response to injury, reduction in the number of circulating lymphocytes, and functioning of the central nervous system. [NIH]

Glutamate: Excitatory neurotransmitter of the brain. [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]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Glycosaminoglycans: Heteropolysaccharides which contain an N-acetylated hexosamine in a characteristic repeating disaccharide unit. The repeating structure of each disaccharide involves alternate 1,4- and 1,3-linkages consisting of either N-acetylglucosamine or N-acetylgalactosamine. [NIH]

Goats: Any of numerous agile, hollow-horned ruminants of the genus Capra, closely related to the sheep. [NIH]

Gonadal: Pertaining to a gonad. [EU]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [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]

Grafting: The operation of transfer of tissue from one site to another. [NIH]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Granulosa Cells: Cells of the membrana granulosa lining the vesicular ovarian follicle which become luteal cells after ovulation. [NIH]

Grasses: A large family, Gramineae, of narrow-leaved herbaceous monocots. Many grasses produce highly allergenic pollens and are hosts to cattle parasites and toxic fungi. [NIH]

Growth: The progressive development of a living being or part of an organism from its earliest stage to maturity. [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]

Hair follicles: Shafts or openings on the surface of the skin through which hair grows. [NIH]

Handedness: Preference for using right or left hand. [NIH]

Headache: Pain in the cranial region that may occur as an isolated and benign symptom or as a manifestation of a wide variety of conditions including subarachnoid hemorrhage; craniocerebral trauma; central nervous system infections; intracranial hypertension; and other disorders. In general, recurrent headaches that are not associated with a primary disease process are referred to as headache disorders (e.g., migraine). [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]

Hearing aid: A miniature, portable sound amplifier for persons with impaired hearing, consisting of a microphone, audio amplifier, earphone, and battery. [NIH]

Hearing Disorders: Conditions that impair the transmission or perception of auditory impulses and information from the level of the ear to the temporal cortices, including the sensorineural pathways. [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]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Hemostasis: The process which spontaneously arrests the flow of blood from vessels carrying blood under pressure. It is accomplished by contraction of the vessels, adhesion and aggregation of formed blood elements, and the process of blood or plasma coagulation.

[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]

Heterodimers: Zippered pair of nonidentical proteins. [NIH]

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]

Heterogenic: Derived from a different source or species. Also called heterogenous. [NIH]

Heterogenous: Derived from a different source or species. Also called heterogenic. [NIH]

Heterozygotes: Having unlike alleles at one or more corresponding loci on homologous chromosomes. [NIH]

Homeobox: Distinctive sequence of DNA bases. [NIH]

Homogeneous: Consisting of or composed of similar elements or ingredients; of a uniform quality throughout. [EU]

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]

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]

Host: Any animal that receives a transplanted graft. [NIH]

Human Development: Continuous sequential changes which occur in the physiological and psychological functions during the individual's life. [NIH]

Hybrid: Cross fertilization between two varieties or, more usually, two species of vines, see also crossing. [NIH]

Hybridization: The genetic process of crossbreeding to produce a hybrid. Hybrid nucleic acids can be formed by nucleic acid hybridization of DNA and RNA molecules. Protein hybridization allows for hybrid proteins to be formed from polypeptide chains. [NIH]

Hydrocephalus: Excessive accumulation of cerebrospinal fluid within the cranium which may be associated with dilation of cerebral ventricles, intracranial hypertension; headache; lethargy; urinary incontinence; and ataxia (and in infants macrocephaly). This condition may be caused by obstruction of cerebrospinal fluid pathways due to neurologic abnormalities, intracranial hemorrhages; central nervous system infections; brain neoplasms; craniocerebral trauma; and other conditions. Impaired resorption of cerebrospinal fluid from the arachnoid villi results in a communicating form of hydrocephalus. Hydrocephalus ex-vacuo refers to ventricular dilation that occurs as a result of brain substance loss from cerebral infarction and other conditions. [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]

Hydrops Fetalis: Edema of the entire body due to abnormal accumulation of serous fluid in the tissues, associated with severe anemia and occurring in fetal erythroblastosis. [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]

Hyperlipoproteinemia: Metabolic disease characterized by elevated plasma cholesterol and/or triglyceride levels. The inherited form is attributed to a single gene mechanism. [NIH]

Hypertriglyceridemia: Condition of elevated triglyceride concentration in the blood; an inherited form occurs in familial hyperlipoproteinemia IIb and hyperlipoproteinemia type IV. It has been linked to higher risk of heart disease and arteriosclerosis. [NIH]

Hypertrophy: General increase in bulk of a part or organ, not due to tumor formation, nor to an increase in the number of cells. [NIH]

Hypophyseal: Hypophysial. [EU]

Hypoplasia: Incomplete development or underdevelopment of an organ or tissue. [EU]

Hypothalamic: Of or involving the hypothalamus. [EU]

Hypothalamus: Ventral part of the diencephalon extending from the region of the optic chiasm to the caudal border of the mammillary bodies and forming the inferior and lateral walls of the third ventricle. [NIH]

Hypothyroidism: Deficiency of thyroid activity. In adults, it is most common in women and is characterized by decrease in basal metabolic rate, tiredness and lethargy, sensitivity to cold, and menstrual disturbances. If untreated, it progresses to full-blown myxoedema. In infants, severe hypothyroidism leads to cretinism. In juveniles, the manifestations are intermediate, with less severe mental and developmental retardation and only mild symptoms of the adult form. When due to pituitary deficiency of thyrotropin secretion it is called secondary hypothyroidism. [EU]

Hypotonia: A condition of diminished tone of the skeletal muscles; diminished resistance of muscles to passive stretching. [EU]

Hypoxia: Reduction of oxygen supply to tissue below physiological levels despite adequate perfusion of the tissue by blood. [EU]

Iatrogenic: Resulting from the activity of physicians. Originally applied to disorders induced in the patient by autosuggestion based on the physician's examination, manner, or discussion, the term is now applied to any adverse condition in a patient occurring as the result of treatment by a physician or surgeon, especially to infections acquired by the patient during the course of treatment. [EU]

Id: The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Imidazole: C3H4N2. The ring is present in polybenzimidazoles. [NIH]

Immaturity: The state or quality of being unripe or not fully developed. [EU]

Immune response: The activity of the immune system against foreign substances (antigens). [NIH]

Immune system: The organs, cells, and molecules responsible for the recognition and disposal of foreign ("non-self") material which enters the body. [NIH]

Immunoglobulin: A protein that acts as an antibody. [NIH]

Immunohistochemistry: Histochemical localization of immunoreactive substances using labeled antibodies as reagents. [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]

Immunology: The study of the body's immune system. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [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]

Incisor: Anything adapted for cutting; any one of the four front teeth in each jaw. [NIH]

Incompetence: Physical or mental inadequacy or insufficiency. [EU]

Incontinence: Inability to control the flow of urine from the bladder (urinary incontinence) or the escape of stool from the rectum (fecal incontinence). [NIH]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

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]

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]

Infertility: The diminished or absent ability to conceive or produce an offspring while sterility is the complete inability to conceive or produce an offspring. [NIH]

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]

Inhibin: Glyceroprotein hormone produced in the seminiferous tubules by the Sertoli cells in the male and by the granulosa cells in the female follicles. The hormone inhibits FSH and LH synthesis and secretion by the pituitary cells thereby affecting sexual maturation and fertility. [NIH]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a

step in a carcinogenic process. [NIH]

Inner ear: The labyrinth, comprising the vestibule, cochlea, and semicircular canals. [NIH]

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]

Integrins: A family of transmembrane glycoproteins consisting of noncovalent heterodimers. They interact with a wide variety of ligands including extracellular matrix glycoproteins, complement, and other cells, while their intracellular domains interact with the cytoskeleton. The integrins consist of at least three identified families: the cytoadhesin receptors, the leukocyte adhesion receptors, and the very-late-antigen receptors. Each family contains a common beta-subunit combined with one or more distinct alpha-subunits. These receptors participate in cell-matrix and cell-cell adhesion in many physiologically important processes, including embryological development, hemostasis, thrombosis, wound healing, immune and nonimmune defense mechanisms, and oncogenic transformation. [NIH]

Interphase: The interval between two successive cell divisions during which the chromosomes are not individually distinguishable and DNA replication occurs. [NIH]

Interstitial: Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

Intestinal: Having to do with the intestines. [NIH]

Intestines: The section of the alimentary canal from the stomach to the anus. It includes the large intestine and small intestine. [NIH]

Intoxication: Poisoning, the state of being poisoned. [EU]

Intracellular: Inside a cell. [NIH]

Intracranial Hemorrhages: Bleeding within the intracranial cavity, including hemorrhages in the brain and within the cranial epidural, subdural, and subarachnoid spaces. [NIH]

Intracranial Hypertension: Increased pressure within the cranial vault. This may result from several conditions, including hydrocephalus; brain edema; intracranial masses; severe systemic hypertension; pseudotumor cerebri; and other disorders. [NIH]

Intraocular: Within the eye. [EU]

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]

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]

Iris: The most anterior portion of the uveal layer, separating the anterior chamber from the posterior. It consists of two layers - the stroma and the pigmented epithelium. Color of the iris depends on the amount of melanin in the stroma on reflection from the pigmented epithelium. [NIH]

Joint: The point of contact between elements of an animal skeleton with the parts that surround and support it. [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]

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]

Lacrimal: Pertaining to the tears. [EU]

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]

Language Development: The gradual expansion in complexity and meaning of symbols and sounds as perceived and interpreted by the individual through a maturational and learning process. Stages in development include babbling, cooing, word imitation with cognition, and use of short sentences. [NIH]

Language Development Disorders: Conditions characterized by language abilities (comprehension and expression of speech and writing) that are below the expected level for a given age, generally in the absence of an intellectual impairment. These conditions may be associated with deafness; brain diseases; mental disorders; or environmental factors. [NIH]

Language Disorders: Conditions characterized by deficiencies of comprehension or expression of written and spoken forms of language. These include acquired and developmental disorders. [NIH]

Language Therapy: Rehabilitation of persons with language disorders or training of children with language development disorders. [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]

Laryngeal: Having to do with the larynx. [NIH]

Laryngectomy: Total or partial excision of the larynx. [NIH]

Larynx: An irregularly shaped, musculocartilaginous tubular structure, lined with mucous membrane, located at the top of the trachea and below the root of the tongue and the hyoid bone. It is the essential sphincter guarding the entrance into the trachea and functioning secondarily as the organ of voice. [NIH]

Lens: The transparent, double convex (outward curve on both sides) structure suspended between the aqueous and vitreous; helps to focus light on the retina. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Lethal: Deadly, fatal. [EU]

Lethargy: Abnormal drowsiness or stupor; a condition of indifference. [EU]

Leukotrienes: A family of biologically active compounds derived from arachidonic acid by oxidative metabolism through the 5-lipoxygenase pathway. They participate in host defense reactions and pathophysiological conditions such as immediate hypersensitivity and inflammation. They have potent actions on many essential organs and systems, including the cardiovascular, pulmonary, and central nervous system as well as the gastrointestinal tract and the immune system. [NIH]

Library Services: Services offered to the library user. They include reference and circulation. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and strengthen joints. [EU]

Ligands: A RNA simulation method developed by the MIT. [NIH]

Limb Bud: A swelling on the trunk of the vertebrate embryo that becomes a limb. Limb bud

cultures are used in developmental, organogenesis, morphogenesis, and cell differentiation studies. The limb bud of the chick embryo is most commonly used but mouse and rat limb buds are also used. [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]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [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]

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]

Loop: A wire usually of platinum bent at one end into a small loop (usually 4 mm inside diameter) and used in transferring microorganisms. [NIH]

Lower Esophageal Sphincter: The muscle between the esophagus and stomach. When a person swallows, this muscle relaxes to let food pass from the esophagus to the stomach. It stays closed at other times to keep stomach contents from flowing back into the esophagus. [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]

Lung volume: The amount of air the lungs hold. [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]

Lymphedema: Edema due to obstruction of lymph vessels or disorders of the lymph nodes. [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]

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]

Malformation: A morphologic defect resulting from an intrinsically abnormal developmental process. [EU]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Mammary: Pertaining to the mamma, or breast. [EU]

Mandible: The largest and strongest bone of the face constituting the lower jaw. It supports the lower teeth. [NIH]

Mastication: The act and process of chewing and grinding food in the mouth. [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]

Maxillary: Pertaining to the maxilla : the irregularly shaped bone that with its fellow forms the upper jaw. [EU]

Meatus: A canal running from the internal auditory foramen through the petrous portion of the temporal bone. It gives passage to the facial and auditory nerves together with the auditory branch of the basilar artery and the internal auditory veins. [NIH]

Mechlorethamine: A vesicant and necrotizing irritant destructive to mucous membranes. It was formerly used as a war gas. The hydrochloride is used as an antineoplastic in Hodgkin's disease and lymphomas. It causes severe gastrointestinal and bone marrow damage. [NIH]

Medial: Lying near the midsaggital plane of the body; opposed to lateral. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

Medical Records: Recording of pertinent information concerning patient's illness or illnesses. [NIH]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Megaloblastic: A large abnormal red blood cell appearing in the blood in pernicious anaemia. [EU]

Melanin: The substance that gives the skin its color. [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]

Meninges: The three membranes that cover and protect the brain and spinal cord. [NIH]

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]

Mental Processes: Conceptual functions or thinking in all its forms. [NIH]

Mental Retardation: Refers to sub-average general intellectual functioning which originated during the developmental period and is associated with impairment in adaptive behavior. [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]

Mesenchymal: Refers to cells that develop into connective tissue, blood vessels, and lymphatic tissue. [NIH]

Mesoderm: The middle germ layer of the embryo. [NIH]

Metabolite: Any substance produced by metabolism or by a metabolic process. [EU]

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]

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]

Microcirculation: The vascular network lying between the arterioles and venules; includes capillaries, metarterioles and arteriovenous anastomoses. Also, the flow of blood through this network. [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]

Microscopy: The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

Migration: The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

Mineralocorticoids: A group of corticosteroids primarily associated with the regulation of water and electrolyte balance. This is accomplished through the effect on ion transport in renal tubules, resulting in retention of sodium and loss of potassium. Mineralocorticoid secretion is itself regulated by plasma volume, serum potassium, and angiotensin II. [NIH]

Mitosis: A method of indirect cell division by means of which the two daughter nuclei normally receive identical complements of the number of chromosomes of the somatic cells of the species. [NIH]

Mitral Valve: The valve between the left atrium and left ventricle of the heart. [NIH]

Mitral Valve Prolapse: Abnormal protrusion of one or both of the leaflets of the mitral valve into the left atrium during systole. This may be accompanied by mitral regurgitation, systolic murmur, nonejection click, or cardiac arrhythmia. [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]

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]

Monosomy: The condition in which one chromosome of a pair is missing. In a normally diploid cell it is represented symbolically as 2N-1. [NIH]

Morphogenesis: The development of the form of an organ, part of the body, or organism. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Morphology: The science of the form and structure of organisms (plants, animals, and other forms of life). [NIH]

Motor Skills: Performance of complex motor acts. [NIH]

Mucociliary: Pertaining to or affecting the mucus membrane and hairs (including eyelashes, nose hair, .): mucociliary clearing: the clearance of mucus by ciliary movement (particularly in the respiratory system). [EU]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Muscle Fibers: Large single cells, either cylindrical or prismatic in shape, that form the basic unit of muscle tissue. They consist of a soft contractile substance enclosed in a tubular sheath. [NIH]

Muscular Dystrophies: A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

Musculoskeletal System: Themuscles, bones, and cartilage of the body. [NIH]

Mutagenesis: Process of generating genetic mutations. It may occur spontaneously or be induced by mutagens. [NIH]

Mutagens: Chemical agents that increase the rate of genetic mutation by interfering with the function of nucleic acids. A clastogen is a specific mutagen that causes breaks in chromosomes. [NIH]

Mutism: Inability or refusal to speak. [EU]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Nasal Cavity: The proximal portion of the respiratory passages on either side of the nasal septum, lined with ciliated mucosa, extending from the nares to the pharynx. [NIH]

Nasal Mucosa: The mucous membrane lining the nasal cavity. [NIH]

Nasopharynx: The nasal part of the pharynx, lying above the level of the soft palate. [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]

Need: A state of tension or dissatisfaction felt by an individual that impels him to action toward a goal he believes will satisfy the impulse. [NIH]

Neonatal: Pertaining to the first four weeks after birth. [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]

Networks: Pertaining to a nerve or to the nerves, a meshlike structure of interlocking fibers or strands. [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]

Neural Crest: A strip of specialized ectoderm flanking each side of the embryonal neural plate, which after the closure of the neural tube, forms a column of isolated cells along the dorsal aspect of the neural tube. Most of the cranial and all of the spinal sensory ganglion cells arise by differentiation of neural crest cells. [NIH]

Neural tube defects: These defects include problems stemming from fetal development of the spinal cord, spine, brain, and skull, and include birth defects such as spina bifida, anencephaly, and encephalocele. Neural tube defects occur early in pregnancy at about 4 to 6 weeks, usually before a woman knows she is pregnant. Many babies with neural tube defects have difficulty walking and with bladder and bowel control. [NIH]

Neurologic: Having to do with nerves or the nervous system. [NIH]

Neuroma: A tumor that arises in nerve cells. [NIH]

Neuromuscular: Pertaining to muscles and nerves. [EU]

Neuronal: Pertaining to a neuron or neurons (= conducting cells of the nervous system). [EU]

Neurons: The basic cellular units of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system. [NIH]

Neuropsychological Tests: Tests designed to assess neurological function associated with certain behaviors. They are used in diagnosing brain dysfunction or damage and central nervous system disorders or injury. [NIH]

Nickel: A trace element with the atomic symbol Ni, atomic number 28, and atomic weight 58.69. It is a cofactor of the enzyme urease. [NIH]

Nipples: The conic organs which usually give outlet to milk from the mammary glands. [NIH]

Nonverbal Communication: Transmission of emotions, ideas, and attitudes between individuals in ways other than the spoken language. [NIH]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [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]

Nucleic Acid Hybridization: The process whereby two single-stranded polynucleotides form a double-stranded molecule, with hydrogen bonding between the complementary bases in the two strains. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Occult: Obscure; concealed from observation, difficult to understand. [EU]

Ocular: 1. Of, pertaining to, or affecting the eye. 2. Eyepiece. [EU]

Odour: A volatile emanation that is perceived by the sense of smell. [EU]

Oncogenic: Chemical, viral, radioactive or other agent that causes cancer; carcinogenic. [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]

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]

Orbicularis: A thin layer of fibers that originates at the posterior lacrimal crest and passes outward and forward, dividing into two slips which surround the canaliculi. [NIH]

Organ Culture: The growth in aseptic culture of plant organs such as roots or shoots, beginning with organ primordia or segments and maintaining the characteristics of the organ. [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]

Orthopedics: A surgical specialty which utilizes medical, surgical, and physical methods to treat and correct deformities, diseases, and injuries to the skeletal system, its articulations, and associated structures. [NIH]

Osseointegration: The growth action of bone tissue, as it assimilates surgically implanted devices or prostheses to be used as either replacement parts (e.g., hip) or as anchors (e.g., endosseous dental implants). [NIH]

Ossification: The formation of bone or of a bony substance; the conversion of fibrous tissue or of cartilage into bone or a bony substance. [EU]

Osteogenesis: The histogenesis of bone including ossification. It occurs continuously but particularly in the embryo and child and during fracture repair. [NIH]

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]

Otitis Media with Effusion: Inflammation of the middle ear with a clear pale yellow-

colored transudate. [NIH]

Otolaryngologist: A doctor who specializes in treating diseases of the ear, nose, and throat. Also called an ENT doctor. [NIH]

Otolaryngology: A surgical specialty concerned with the study and treatment of disorders of the ear, nose, and throat. [NIH]

Outer ear: The pinna and external meatus of the ear. [NIH]

Ovaries: The pair of female reproductive glands in which the ova, or eggs, are formed. The ovaries are located in the pelvis, one on each side of the uterus. [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]

Paediatric: Of or relating to the care and medical treatment of children; belonging to or concerned with paediatrics. [EU]

Palatal Muscles: The muscles of the palate are the glossopalatine, palatoglossus, levator palati(ni), musculus uvulae, palatopharyngeus, and tensor palati(ni). [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]

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]

Pancreatic: Having to do with the pancreas. [NIH]

Pancreatic Juice: The fluid containing digestive enzymes secreted by the pancreas in response to food in the duodenum. [NIH]

Paranasal Sinuses: Air-filled extensions of the respiratory part of the nasal cavity into the frontal, ethmoid, sphenoid, and maxillary cranial bones. They vary in size and form in different individuals and are lined by the ciliated mucous membranes of the nasal cavity. [NIH]

Parathyroid: 1. Situated beside the thyroid gland. 2. One of the parathyroid glands. 3. A sterile preparation of the water-soluble principle(s) of the parathyroid glands, ad-ministered parenterally as an antihypocalcaemic, especially in the treatment of acute hypoparathyroidism with tetany. [EU]

Parathyroid Glands: Two small paired endocrine glands in the region of the thyroid gland. They secrete parathyroid hormone and are concerned with the metabolism of calcium and phosphorus. [NIH]

Parathyroid hormone: A substance made by the parathyroid gland that helps the body store and use calcium. Also called parathormone, parathyrin, or PTH. [NIH]

Particle: A tiny mass of material. [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]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

Pathophysiology: Altered functions in an individual or an organ due to disease. [NIH]

Patient Advocacy: Promotion and protection of the rights of patients, frequently through a legal process. [NIH]

Patient Care Team: Care of patients by a multidisciplinary team usually organized under the leadership of a physician; each member of the team has specific responsibilities and the whole team contributes to the care of the patient. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Peptic: Pertaining to pepsin or to digestion; related to the action of gastric juices. [EU]

Peptic Ulcer: Ulcer that occurs in those portions of the alimentary tract which come into contact with gastric juice containing pepsin and acid. It occurs when the amount of acid and pepsin is sufficient to overcome the gastric mucosal barrier. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make 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]

Perforation: 1. The act of boring or piercing through a part. 2. A hole made through a part or substance. [EU]

Perfusion: Bathing an organ or tissue with a fluid. In regional perfusion, a specific area of the body (usually an arm or a leg) receives high doses of anticancer drugs through a blood vessel. Such a procedure is performed to treat cancer that has not spread. [NIH]

Perinatal: Pertaining to or occurring in the period shortly before and after birth; variously defined as beginning with completion of the twentieth to twenty-eighth week of gestation and ending 7 to 28 days after birth. [EU]

Peroral: Performed through or administered through the mouth. [EU]

Pharmacologic: Pertaining to pharmacology or to the properties and reactions of drugs. [EU]

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]

Phenylalanine: An aromatic amino acid that is essential in the animal diet. It is a precursor of melanin, dopamine, noradrenalin, and thyroxine. [NIH]

Phocomelia: Congenital deformity that leaves the child without legs. [NIH]

Phonation: The process of producing vocal sounds by means of vocal cords vibrating in an expiratory blast of air. [NIH]

Phospholipases: A class of enzymes that catalyze the hydrolysis of phosphoglycerides or glycerophosphatidates. EC 3.1.-. [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]

Physical Examination: Systematic and thorough inspection of the patient for physical signs of disease or abnormality. [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]

Pilot study: The initial study examining a new method or treatment. [NIH]

Pitch: The subjective awareness of the frequency or spectral distribution of a sound. [NIH]

Pituitary Gland: A small, unpaired gland situated in the sella turcica tissue. It is connected to the hypothalamus by a short stalk. [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]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plastic surgeon: A surgeon who specializes in reducing scarring or disfigurement that may occur as a result of accidents, birth defects, or treatment for diseases. [NIH]

Platelet Activation: A series of progressive, overlapping events triggered by exposure of the platelets to subendothelial tissue. These events include shape change, adhesiveness, aggregation, and release reactions. When carried through to completion, these events lead to the formation of a stable hemostatic plug. [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]

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]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

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]

Pons: The part of the central nervous system lying between the medulla oblongata and the mesencephalon, ventral to the cerebellum, and consisting of a pars dorsalis and a pars ventralis. [NIH]

Port: An implanted device through which blood may be withdrawn and drugs may be infused without repeated needle sticks. Also called a port-a-cath. [NIH]

Port-a-cath: An implanted device through which blood may be withdrawn and drugs may

be infused without repeated needle sticks. Also called a port. [NIH]

Posterior: Situated in back of, or in the back part of, or affecting the back or dorsal surface of the body. In lower animals, it refers to the caudal end of the body. [EU]

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]

Postoperative: After surgery. [NIH]

Postsynaptic: Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

Potentiation: An overall effect of two drugs taken together which is greater than the sum of the effects of each drug taken alone. [NIH]

Practicability: A non-standard characteristic of an analytical procedure. It is dependent on the scope of the method and is determined by requirements such as sample throughout and costs. [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]

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]

Prednisone: A synthetic anti-inflammatory glucocorticoid derived from cortisone. It is biologically inert and converted to prednisolone in the liver. [NIH]

Pregnancy Tests: Tests to determine whether or not an individual is pregnant. [NIH]

Prenatal: Existing or occurring before birth, with reference to the fetus. [EU]

Prenatal Diagnosis: Determination of the nature of a pathological condition or disease in the postimplantation embryo, fetus, or pregnant female before birth. [NIH]

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]

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]

Procarbazine: An antineoplastic agent used primarily in combination with mechlorethamine, vincristine, and prednisone (the MOPP protocol) in the treatment of Hodgkin's disease. [NIH]

Progesterone: Pregn-4-ene-3,20-dione. The principal progestational hormone of the body, secreted by the corpus luteum, adrenal cortex, and placenta. Its chief function is to prepare the uterus for the reception and development of the fertilized ovum. It acts as an antiovulatory agent when administered on days 5-25 of the menstrual cycle. [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]

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]

Prostaglandin: Any of a group of components derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway that are extremely potent mediators of a diverse group of physiologic processes. The abbreviation for prostaglandin is PG; specific compounds are designated by adding one of the letters A through I to indicate the type of substituents found on the hydrocarbon skeleton and a subscript (1, 2 or 3) to indicate the number of double bonds in the hydrocarbon skeleton e.g., PGE2. The predominant naturally occurring prostaglandins all have two double bonds and are synthesized from arachidonic acid (5,8,11,14-eicosatetraenoic acid) by the pathway shown in the illustration. The 1 series and 3 series are produced by the same pathway with fatty acids having one fewer double bond (8,11,14-eicosatrienoic acid or one more double bond (5,8,11,14,17-eicosapentaenoic acid) than arachidonic acid. The subscript a or ß indicates the configuration at C-9 (a denotes a substituent below the plane of the ring, ß, above the plane). The naturally occurring PGF's have the a configuration, e.g., PGF2a. All of the prostaglandins act by binding to specific cell-surface receptors causing an increase in the level of the intracellular second messenger cyclic AMP (and in some cases cyclic GMP also). The effect produced by the cyclic AMP increase depends on the specific cell type. In some cases there is also a positive feedback effect. Increased cyclic AMP increases prostaglandin synthesis leading to further increases in cyclic AMP. [EU]

Prostaglandin-Endoperoxide Synthase: An enzyme complex that catalyzes the formation of prostaglandins from the appropriate unsaturated fatty acid, molecular oxygen, and a reduced acceptor. EC 1.14.99.1. [NIH]

Prostaglandins A: (13E,15S)-15-Hydroxy-9-oxoprosta-10,13-dien-1-oic acid (PGA(1)); (5Z,13E,15S)-15-hydroxy-9-oxoprosta-5,10,13-trien-1-oic acid (PGA(2)); (5Z,13E,15S,17Z)-15-hydroxy-9-oxoprosta-5,10,13,17-tetraen-1-oic acid (PGA(3)). A group of naturally occurring secondary prostaglandins derived from PGE. PGA(1) and PGA(2) as well as their 19-hydroxy derivatives are found in many organs and tissues. [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]

Prosthesis: An artificial replacement of a part of the body. [NIH]

Prosthodontics: A dental specialty concerned with the restoration and maintenance of oral function by the replacement of missing teeth and structures by artificial devices or prostheses. [NIH]

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 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]

Proteoglycans: Glycoproteins which have a very high polysaccharide content. [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]

Proximal: Nearest; closer to any point of reference; opposed to distal. [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]

Psychology: The science dealing with the study of mental processes and behavior in man and animals. [NIH]

Psychomotor: Pertaining to motor effects of cerebral or psychic activity. [EU]

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 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]

Pulmonary Ventilation: The total volume of gas per minute inspired or expired measured in liters per minute. [NIH]

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]

Quiescent: Marked by a state of inactivity or repose. [EU]

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]

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]

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]

Radiologist: A doctor who specializes in creating and interpreting pictures of areas inside the body. The pictures are produced with x-rays, sound waves, or other types of energy. [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 Controlled Trials: Clinical trials that involve at least one test treatment and one control treatment, concurrent enrollment and follow-up of the test- and control-treated groups, and in which the treatments to be administered are selected by a random process, such as the use of a random-numbers table. Treatment allocations using coin flips, odd-even numbers, patient social security numbers, days of the week, medical record numbers, or other such pseudo- or quasi-random processes, are not truly randomized and trials employing any of these techniques for patient assignment are designated simply controlled clinical trials. [NIH]

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]

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]

Recurrence: The return of a sign, symptom, or disease after a remission. [NIH]

Reductase: Enzyme converting testosterone to dihydrotestosterone. [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]

Regurgitation: A backward flowing, as the casting up of undigested food, or the backward flowing of blood into the heart, or between the chambers of the heart when a valve is incompetent. [EU]

Remission: A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although there still may be cancer in the body. [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]

Research Design: A plan for collecting and utilizing data so that desired information can be obtained with sufficient precision or so that an hypothesis can be tested properly. [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]

Respiratory System: The tubular and cavernous organs and structures, by means of which pulmonary ventilation and gas exchange between ambient air and the blood are brought about. [NIH]

Restoration: Broad term applied to any inlay, crown, bridge or complete denture which restores or replaces loss of teeth or oral tissues. [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]

Retrospective: Looking back at events that have already taken place. [NIH]

Retrospective study: A study that looks backward in time, usually using medical records and interviews with patients who already have or had a disease. [NIH]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Sagittal: The line of direction passing through the body from back to front, or any vertical plane parallel to the medial plane of the body and inclusive of that plane; often restricted to the medial plane, the plane of the sagittal suture. [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]

Saponins: Sapogenin glycosides. A type of glycoside widely distributed in plants. Each consists of a sapogenin as the aglycon moiety, and a sugar. The sapogenin may be a steroid or a triterpene and the sugar may be glucose, galactose, a pentose, or a methylpentose. Sapogenins are poisonous towards the lower forms of life and are powerful hemolytics when injected into the blood stream able to dissolve red blood cells at even extreme dilutions. [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]

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]

Screening: Checking for disease when there are no symptoms. [NIH]

Scrotum: In males, the external sac that contains the testicles. [NIH]

Sebaceous: Gland that secretes sebum. [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]

Segmental: Describing or pertaining to a structure which is repeated in similar form in successive segments of an organism, or which is undergoing segmentation. [NIH]

Segmentation: The process by which muscles in the intestines move food and wastes through the body. [NIH]

Segregation: The separation in meiotic cell division of homologous chromosome pairs and their contained allelomorphic gene pairs. [NIH]

Seizures: Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena. Recurrent seizures are usually referred to as epilepsy or "seizure disorder." [NIH]

Self-Help Groups: Organizations which provide an environment encouraging social interactions through group activities or individual relationships especially for the purpose of rehabilitating or supporting patients, individuals with common health problems, or the elderly. They include therapeutic social clubs. [NIH]

Semen: The thick, yellowish-white, viscid fluid secretion of male reproductive organs discharged upon ejaculation. In addition to reproductive organ secretions, it contains spermatozoa and their nutrient plasma. [NIH]

Semicircular canal: Three long canals of the bony labyrinth of the ear, forming loops and opening into the vestibule by five openings. [NIH]

Seminiferous tubule: Tube used to transport sperm made in the testes. [NIH]

Senile: Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

Sensibility: The ability to receive, feel and appreciate sensations and impressions; the quality of being sensitive; the extend to which a method gives results that are free from false negatives. [NIH]

Sensor: A device designed to respond to physical stimuli such as temperature, light, magnetism or movement and transmit resulting impulses for interpretation, recording, movement, or operating control. [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]

Serous: Having to do with serum, the clear liquid part of blood. [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]

Sex Ratio: The number of males per 100 females. [NIH]

Shyness: Discomfort and partial inhibition of the usual forms of behavior when in the presence of others. [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]

Signal Transduction: The intercellular or intracellular transfer of information (biological activation/inhibition) through a signal pathway. In each signal transduction system, an

activation/inhibition signal from a biologically active molecule (hormone, neurotransmitter) is mediated via the coupling of a receptor/enzyme to a second messenger system or to an ion channel. Signal transduction plays an important role in activating cellular functions, cell differentiation, and cell proliferation. Examples of signal transduction systems are the GABA-postsynaptic receptor-calcium ion channel system, the receptor-mediated T-cell activation pathway, and the receptor-mediated activation of phospholipases. Those coupled to membrane depolarization or intracellular release of calcium include the receptor-mediated activation of cytotoxic functions in granulocytes and the synaptic potentiation of protein kinase activation. Some signal transduction pathways may be part of larger signal transduction pathways; for example, protein kinase activation is part of the platelet activation signal pathway. [NIH]

Sinusitis: An inflammatory process of the mucous membranes of the paranasal sinuses that occurs in three stages: acute, subacute, and chronic. Sinusitis results from any condition causing ostial obstruction or from pathophysiologic changes in the mucociliary transport mechanism. [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]

Skull: The skeleton of the head including the bones of the face and the bones enclosing the brain. [NIH]

Sleep apnea: A serious, potentially life-threatening breathing disorder characterized by repeated cessation of breathing due to either collapse of the upper airway during sleep or absence of respiratory effort. [NIH]

Small intestine: The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

Social Behavior: Any behavior caused by or affecting another individual, usually of the same species. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

Social Work: The use of community resources, individual case work, or group work to promote the adaptive capacities of individuals in relation to their social and economic environments. It includes social service agencies. [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 Channels: Cell membrane glycoproteins selective for sodium ions. Fast sodium current is associated with the action potential in neural membranes. [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]

Soma: The body as distinct from the mind; all the body tissue except the germ cells; all the axial body. [NIH]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

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]

Soybean Oil: Oil from soybean or soybean plant. [NIH]

Spatial disorientation: Loss of orientation in space where person does not know which way is up. [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]

Speech Disorders: Acquired or developmental conditions marked by an impaired ability to comprehend or generate spoken forms of language. [NIH]

Speech pathologist: A specialist who evaluates and treats people with communication and swallowing problems. Also called a speech therapist. [NIH]

Sperm: The fecundating fluid of the male. [NIH]

Sphincter: A ringlike band of muscle fibres that constricts a passage or closes a natural orifice; called also musculus sphincter. [EU]

Spina bifida: A defect in development of the vertebral column in which there is a central deficiency of the vertebral lamina. [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]

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]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Stem Cells: Relatively undifferentiated cells of the same lineage (family type) that retain the ability to divide and cycle throughout postnatal life to provide cells that can become specialized and take the place of those that die or are lost. [NIH]

Sterile: Unable to produce children. [NIH]

Sterility: 1. The inability to produce offspring, i.e., the inability to conceive (female s.) or to induce conception (male s.). 2. The state of being aseptic, or free from microorganisms. [EU]

Steroid: A group name for lipids that contain a hydrogenated cyclopentanoperhydrophenanthrene ring system. Some of the substances included in this group are progesterone, adrenocortical hormones, the gonadal hormones, cardiac aglycones,

bile acids, sterols (such as cholesterol), toad poisons, saponins, and some of the carcinogenic hydrocarbons. [EU]

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]

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]

Stroma: The middle, thickest layer of tissue in the cornea. [NIH]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subcutaneous: Beneath the skin. [NIH]

Submandibular: Four to six lymph glands, located between the lower jaw and the submandibular salivary gland. [NIH]

Submucous: Occurring beneath the mucosa or a mucous membrane. [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]

Superstitions: A belief or practice which lacks adequate basis for proof; an embodiment of fear of the unknown, magic, and ignorance. [NIH]

Supplementation: Adding nutrients to the diet. [NIH]

Support group: A group of people with similar disease who meet to discuss how better to cope with their cancer and treatment. [NIH]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Symphysis: A secondary cartilaginous joint. [NIH]

Synaptic: Pertaining to or affecting a synapse (= site of functional apposition between neurons, at which an impulse is transmitted from one neuron to another by electrical or chemical means); pertaining to synapsis (= pairing off in point-for-point association of homologous chromosomes from the male and female pronuclei during the early prophase of meiosis). [EU]

Synechia: Adhesion of the iris to the cornea or to the capsule of the crystalline lens. [NIH]

Systole: Period of contraction of the heart, especially of the ventricles. [NIH]

Systolic: Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

Temporal: One of the two irregular bones forming part of the lateral surfaces and base of the skull, and containing the organs of hearing. [NIH]

Teratogen: A substance which, through immediate, prolonged or repeated contact with the skin may involve a risk of subsequent non-hereditable birth defects in offspring. [NIH]

Teratogenic: Tending to produce anomalies of formation, or teratism (= anomaly of

formation or development : condition of a monster). [EU]

Teratoma: A type of germ cell tumor that may contain several different types of tissue, such as hair, muscle, and bone. Teratomas occur most often in the ovaries in women, the testicles in men, and the tailbone in children. Not all teratomas are malignant. [NIH]

Testicles: The two egg-shaped glands found inside the scrotum. They produce sperm and male hormones. Also called testes. [NIH]

Testicular: Pertaining to a testis. [EU]

Testosterone: A hormone that promotes the development and maintenance of male sex characteristics. [NIH]

Tetany: 1. Hyperexcitability of nerves and muscles due to decrease in concentration of extracellular ionized calcium, which may be associated with such conditions as parathyroid hypofunction, vitamin D deficiency, and alkalosis or result from ingestion of alkaline salts; it is characterized by carpopedal spasm, muscular twitching and cramps, laryngospasm with inspiratory stridor, hyperreflexia and choreiform movements. 2. Tetanus. [EU]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombocytopenia: A decrease in the number of blood platelets. [NIH]

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]

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]

Thyroid Gland: A highly vascular endocrine gland consisting of two lobes, one on either side of the trachea, joined by a narrow isthmus; it produces the thyroid hormones which are concerned in regulating the metabolic rate of the body. [NIH]

Thyrotropin: A peptide hormone secreted by the anterior pituitary. It promotes the growth of the thyroid gland and stimulates the synthesis of thyroid hormones and the release of thyroxine by the thyroid gland. [NIH]

Time Factors: Elements of limited time intervals, contributing to particular results or situations. [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]

Tonicity: The normal state of muscular tension. [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]

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]

Traction: The act of pulling. [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]

Transforming Growth Factor alpha: Factor isolated in a variety of tissues including epithelium, and maternal decidua. It is closely related to epidermal growth factor and binds to the EGF receptor. TGF-alpha acts synergistically with TGF-beta in inducing phenotypic transformation, but its physiological role is unknown. [NIH]

Transfusion: The infusion of components of blood or whole blood into the bloodstream. The blood may be donated from another person, or it may have been taken from the person earlier and stored until needed. [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]

Treatment Outcome: Evaluation undertaken to assess the results or consequences of management and procedures used in combating disease in order to determine the efficacy, effectiveness, safety, practicability, etc., of these interventions in individual cases or series. [NIH]

Triglyceride: A lipid carried through the blood stream to tissues. Most of the body's fat tissue is in the form of triglycerides, stored for use as energy. Triglycerides are obtained primarily from fat in foods. [NIH]

Trisomy: The possession of a third chromosome of any one type in an otherwise diploid cell. [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]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is

also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

Ubiquitin: A highly conserved 76 amino acid-protein found in all eukaryotic cells. [NIH]

Ultrasonography: The visualization of deep structures of the body by recording the reflections of echoes of pulses of ultrasonic waves directed into the tissues. Use of ultrasound for imaging or diagnostic purposes employs frequencies ranging from 1.6 to 10 megahertz. [NIH]

Unconscious: Experience which was once conscious, but was subsequently rejected, as the "personal unconscious". [NIH]

Urethane: Antineoplastic agent that is also used as a veterinary anesthetic. It has also been used as an intermediate in organic synthesis. Urethane is suspected to be a carcinogen. [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]

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]

Uvula: Uvula palatinae; specifically, the tongue-like process which projects from the middle of the posterior edge of the soft palate. [NIH]

Valproic Acid: A fatty acid with anticonvulsant properties used in the treatment of epilepsy. The mechanisms of its therapeutic actions are not well understood. It may act by increasing GABA levels in the brain or by altering the properties of voltage dependent sodium channels. [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]

Vein: Vessel-carrying blood from various parts of the body to the heart. [NIH]

Velopharyngeal Insufficiency: Failure of the soft palate to reach the posterior pharyngeal wall. It may be caused by cleft palate surgery, palatal or pharyngeal abnormalities or injury, or neuromuscular dysfunction of the velopharyngeal sphincter. It causes hypernasality of speech. [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]

Ventricular: Pertaining to a ventricle. [EU]

Venules: The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

Vertebrae: A bony unit of the segmented spinal column. [NIH]

Vertebral: Of or pertaining to a vertebra. [EU]

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]

Vestibule: A small, oval, bony chamber of the labyrinth. The vestibule contains the utricle and saccule, organs which are part of the balancing apparatus of the ear. [NIH]

Vestibulocochlear Nerve: The 8th cranial nerve. The vestibulocochlear nerve has a cochlear part (cochlear nerve) which is concerned with hearing and a vestibular part (vestibular nerve) which mediates the sense of balance and head position. The fibers of the cochlear nerve originate from neurons of the spiral ganglion and project to the cochlear nuclei (cochlear nucleus). The fibers of the vestibular nerve arise from neurons of Scarpa's ganglion and project to the vestibular nuclei. [NIH]

Vestibulocochlear Nerve Diseases: Diseases of the vestibular and/or cochlear (acoustic) nerves, which join to form the vestibulocochlear nerve. Vestibular neuritis, cochlear neuritis, and acoustic neuromas are relatively common conditions that affect these nerves. Clinical manifestations vary with which nerve is primarily affected, and include hearing loss, vertigo, and tinnitus. [NIH]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

Villi: The tiny, fingerlike projections on the surface of the small intestine. Villi help absorb nutrients. [NIH]

Vincristine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

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]

Viscera: Any of the large interior organs in any one of the three great cavities of the body, especially in the abdomen. [NIH]

Vital Statistics: Used for general articles concerning statistics of births, deaths, marriages, etc. [NIH]

Vitamin E: Vitamin found largely in plant materials, especially wheat germ, corn, sunflower seed, rapeseed, soybean oils, alfalfa, and lettuce. It is used as an antioxidant in vegetable oils and shortenings. [NIH]

Vitamin U: A vitamin found in green vegetables. It is used in the treatment of peptic ulcers, colitis, and gastritis and has an effect on secretory, acid-forming, and enzymatic functions of the intestinal tract. [NIH]

Vitiligo: A disorder consisting of areas of macular depigmentation, commonly on extensor aspects of extremities, on the face or neck, and in skin folds. Age of onset is often in young adulthood and the condition tends to progress gradually with lesions enlarging and extending until a quiescent state is reached. [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]

Vocal cord: The vocal folds of the larynx. [NIH]

Voice Disorders: Disorders of voice pitch, loudness, or quality. Dysphonia refers to impaired utterance of sounds by the vocal folds. [NIH]

Voice Quality: Voice quality is that component of speech which gives the primary

distinction to a given speaker's voice when pitch and loudness are excluded. It involves both phonatory and resonatory characteristics. Some of the descriptions of voice quality are harshness, breathiness and nasality. [NIH]

Vulgaris: An affection of the skin, especially of the face, the back and the chest, due to chronic inflammation of the sebaceous glands and the hair follicles. [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]

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]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [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]

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