## HEADACHE

### A 3-IN-1 MEDICAL REFERENCE

Medical Dictionary

**Bibliography &** 

Annotated Research Guide

TO INTERNET REFERENCES



# HEADACHE

A MEDICAL DICTIONARY, BIBLIOGRAPHY, AND ANNOTATED RESEARCH GUIDE TO INTERNET REFERENCES



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### Acknowledgements

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

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### 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."<sup>1</sup> 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 headache 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 headache, 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 headache, 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 headache. 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 headache, 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 headache.

The Editors

<sup>&</sup>lt;sup>1</sup> From the NIH, National Cancer Institute (NCI): http://www.cancer.gov/cancerinfo/ten-things-to-know.

### **CHAPTER 1. STUDIES ON HEADACHE**

### Overview

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

### The Combined Health Information Database

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

#### Migraine, Tension-Type Headache and Facial Pain: A Common Intraoral Etiology and Treatment

Source: New York State Dental Journal (NYSDJ). 68(6): 24-26. June-July 2002.

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

Summary: A maxillary (upper jaw) alveolar mucosal inflammation, demonstrated by local tenderness and increased temperature, is present in migraine, tension-type headache and facial pain patients even when the patient is asymptomatic. In this article, the author presents research that shows effective treatment of these conditions with fewer side effects than with standard medication by local anti-inflammatory methods. These alternative methods include chilling, application of anti-inflammatory gel, and

4 Headache

low-level (non cutting) laser. Local treatment also mediates cervical muscle spasm, adding to its overall effectiveness. The author notes that with the exception of cervical muscle hyperactivity (spasm) therapy, the treatments discussed are investigational, performed under the auspices of an Institutional Review Boards. Any dentists treating headaches must be thoroughly familiar with other conditions that can cause cranial symptoms, such as lesional headaches, intracranial bleeds, temporal arteritis, and meningitis, so that they are able to recognize the indications for a timely medical referral. 4 figures. 20 references.

### • Nasal Mucosal Headache Presenting as Orofacial Pain: A Review of the Literature and a Case Report

Source: Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics. 92(2): 180-183. August 2001.

Contact: Available from Mosby, Inc. 6277 Sea Harbor Drive, Orlando, FL 32887-4800. (800) 654-2452 or (407) 345-4000. Website: www.harcourthealth.com.

Summary: Headaches are a significant component of many facial pain syndromes. These facial pain and headache syndromes often have various etiologies (causes), including neurologic (nervous system), vascular (blood system), musculoskeletal (muscles and bones), or combinations of these systems. Referred rhinologic headache, however, can be overlooked as a cause of facial pain in the dental literature. In this article, the authors report a case of nasal (nose) mucosal headache that presented as facial pain. The authors also review the related literature. The authors stress that an understanding of the innervation of the nasal tissues and their interaction with trigeminal pathways (the nerves to the face) is vital when trying to exclude nasal mucosal headache from a differential diagnostic list, which should then lead to proper management or referral. Although uncommon, nasal mucosal headaches such as the case presented here should be included in the differential diagnosis of persistent facial pain and headache, when rhinologic signs and symptoms are present. 2 tables. 23 references.

### Personality Characteristics and Accompanying Symptoms in Temporomandibular Joint Dysfunction, Headache, and Facial Pain

Source: Journal of Orofacial Pain. 14(1): 52-58. Winter 2000.

Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-1881. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. Website: www.quintpub.com.

Summary: Patients with different facial pain or headache pathologies usually complain of numerous accompanying symptoms relative to systemic dysfunctions or to the patient's personality characteristics. This article reports on a study undertaken for three purposes: to determine the prevalence of accompanying symptoms in groups of patients with temporomandibular joint (TMJ) dysfunction and other types of facial pain or headache disorders; to assess the patients' personality characteristics and anxiety levels; and to see whether significant differences were found between the groups. The study included 243 patients who had TMJ intracapsular disorder (TMJ, n = 71), tension type headache (TH, n = 52), migraine (M, n = 68), chronic daily headache (CDH, n = 26), or facial pain disorder as somatoform disorder (FP, n = 26). The presence of 23 symptoms was assessed; the Minnesota Multiphasic Personality Inventory (MMPI) and the Spielberger State and Trait Anxiety Inventory (STAI) were administered. Four different MMPI clusters (depressive, conversive, emotional, coper) were also considered. Results showed that the TMJ group had a lower prevalence of almost all symptoms, significantly lower scores of several MMPI and of state anxiety, and odds ratio values less than 1 for all symptoms except phobias and for emotional, conversive, and depressive MMPI profiles. The FP and CDH groups had the highest prevalence of the majority of symptoms and higher MMPI and STAI scale elevations. The authors conclude that some types of headache and facial pain seem to correlate with the presence of a number of accompanying symptoms and with some changes in personality. These changes are particularly relevant in patients with chronic daily headache and facial pain disorder. In contrast, patients with TMJ intracapsular disorders tended to show a low prevalence of accompanying symptoms and a normal personality profile. 4 figures. 3 tables. 29 references.

#### Retrospective Study of Patients With Cluster Headaches

Source: Oral Surgery, Oral Medicine, Oral Pathology. 73(5): 519-525. May 1992.

Summary: Referred pain in the midface and teeth is a common clinical feature of cluster headache and cluster headache-like disorders. This article reports on 33 cases of cluster headache that met the International Headache Society classification criteria, and that were seen by the authors during a 2-year period. Fourteen (42 percent) of 33 patients who were seen by dental practitioners and who received some form of ineffective dental or pharmalogical treatment are described in the article. Almost 50 percent of the cluster headache patients described received inappropriate dental treatment. The authors hope that this review and retrospective assessment will make the dental practitioner aware of this disorder and provide a broader perspective in the treatment of pain in the orofacial region. The authors also discuss clinical presentation, pathogenesis, and treatment of cluster headaches.

#### • Dental Erosion and Aspirin Headache Powders: A Clinical Report

Source: Journal of Prosthodontics. 9(2): 95-98. June 2000.

Contact: Available from W.B. Saunders Company. Periodicals Department, P.O. Box 628239, Orlando, FL 32862-8239.

Summary: The causes of tooth erosion are varied, but all are associated with a chemical attack on the teeth and a resulting loss of tooth structure. Etiologic (causative) factors related to erosion cited in the literature include bulimia (an eating disorder that involves vomiting), eating acidic foods, soft drink consumption, acid reflux (return of stomach gastric acid to the esophagus and mouth), and swimming, among others. This clinical report suggests that chronic use of headache powders can also be a factor leading to tooth erosion. Erosion occurs when tooth structure is dissolved by chemical action not related to bacterial plaque. The authors describe a case report in which a 38 year old female patient presented with a chief complaint of cold sensitivity in her mandibular teeth. The patient suffered from frequent headaches and had a 3 year history of headache powder use, using as many as 6 doses per day of an over the counter product. Each dose contained 520 mg aspirin, 260 mg acetaminophen, and 32.5 mg caffeine. The patient placed the undissolved headache powder under her tongue (sublingually) to increase the rate of absorption, as a result bathing the mandibular (lower jaw) teeth in an acidic solution of dissolving aspirin. Oral examination revealed severe erosion on the occlusal surfaces of the mandibular molars and premolars and moderate erosion of the mandibular anterior teeth. Less erosion was evident on the maxillary (upper jaw) teeth. The mandibular teeth were prepared for full coronal restorations, followed by placement of acrylic provisionals; after a one month trial period, permanent ceramic restorations were utilized. The patient was cautioned about the potential for tooth

erosion caused by aspirin products and was referred to a physician for treatment of the rebound headaches. 4 figures. 29 references.

### • Dysphagia, Headache, and Dizziness as Symptoms of Cervical Spine Disorders

Source: Revue du Rhumatisme (English Edition). 65(5): 346-351. May 1998.

Summary: This journal article provides health professionals with information on recognizing dysphagia, headache, and dizziness as symptoms of cervical spine disorders. Much evidence points to the causal relationship between dysphagia and lesions of the cervical spine. In many cases, dysphagia is caused by a lesion or bony excrescence arising from the anterior aspect of the cervical spine. Sometimes, dysphagia is caused by anterior cervical disk herniation. Other causes include spondylolisthesis, discal calcification, and trauma-related hyperlordosis of the cervical spine. Conservative treatment is usually recommended. Corticosteroids, nonsteroidal anti-inflammatory drugs, spasm-relieving agents, and precautions during meals are helpful. Evidence that lesions of the cervical spine cause headaches is unclear, although lesions of the atlantooccipital, atlantoaxoidal, and C2-C3 joints resulting from osteoarthritis have been shown to cause headaches. Occipital neuralgia has been reported in patients who have septic or rheumatoid arthritis and ankylosing spondylitis. Cervicogenic headache refers to unilateral pain originating in the neck and radiating to the oculofrontotemporal area. There is no evidence that this type of headache originates in the cervical spine. Dizziness not attributable to vertebrobasilar insufficiency may be caused by cervical spine lesions in some patients; however, an extensive search for other causes is needed. 54 references.

### • Nitroglycerin Ointment for Anal Fissures: Effective Treatment or Just a Headache?

Source: Diseases of the Colon and Rectum. 42(3): 383-385. March 1999.

Contact: Available from Williams and Wilkins. 352 West Camden Street, Baltimore, MD 21201-2436.

Summary: Topical nitrates have been shown to cause nitric oxide mediated relaxation of the internal anal sphincter. Previous reports have suggested the efficacy of nitroglycerin ointment in treating anal fissures. This article reports on a study undertaken to assess the longer term usefulness of this treatment. Thirty three patients who had an anal fissure were treated with topical 0.3 percent nitroglycerin ointment applied to the anoderm three times a day and after bowel movements. Patients were followed up by office visits and telephone calls until symptoms were completely resolved or treatment was noted to be ineffective or intolerable. Of the 33 patients, 16 had acute fissures and 17 had chronic fissures. Nitroglycerin was effective in 9 of 16 acute fissures (56 percent) and 7 of 17 chronic fissures (41 percent). Even when effective, 75 percent of patients reported an adverse reaction, specifically headaches or lightheadedness, or both. However, most of the side effects could be tolerated or controlled, and only 3 patients stopped treatment because side effects were intolerable. The authors conclude that topical nitroglycerin was effective only in approximately half of the patients with an anal fissure. In their experience, nitroglycerin causes a headache more often than it treats the symptoms of anal fissure. 1 table. 14 references. (AA-M).

### Federally Funded Research on Headache

The U.S. Government supports a variety of research studies relating to headache. These studies are tracked by the Office of Extramural Research at the National Institutes of

Health.<sup>2</sup> 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 headache.

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

#### Project Title: A RANDOMIZED TRIAL OF HEADACHE MANAGEMENT PROGRAMS

Principal Investigator & Institution: Harpole, Linda H.; Medicine; Duke University Durham, Nc 27706

Timing: Fiscal Year 2001; Project Start 30-SEP-2001; Project End 29-SEP-2004

Summary: The objective of the proposed study is to determine whether headache management programs should be promoted as an effective and cost- effective strategy for managing patients with chronic disabling headache. The project seeks to translate the current evidence on headache management into clinical practice. Its foundations are the Agency for Healthcare Research and Quality technical reviews on the state-of-thescience in headache management and the practice guidelines based thereon developed by the Headache Guideline Consortium. The functional specifications for the headache management program were developed by an expert advisory panel on headache care, and pilottested in a demonstration project. The demonstration project achieved a reduction in headache-related disability and an improvement in quality of life and patient satisfaction for patients with chronic **headache**. The purpose of the **headache** management program is to assure appropriate headache diagnosis, patient education and activation, clinical treatment and management based upon the evidence-based guidelines, and regular patient monitoring and follow-up. In the proposed study, patients in three geographically and clinically diverse clinical settings, (a managed care organization in Southern California, an academic general internal medicine practice in Pennsylvania and a community-based practice in North Carolina) who are identified by their primary care physicians as having chronic disabling **headache**, will be randomized to usual care or to the headache management program. In total, 828 patients will be enrolled in the study, 414 in the control and 414 in the intervention group. Patients in the intervention arm will be enrolled in the **headache** management program for 6 months. Data collection will be by telephone and mail at baseline and by mail at 3, 6, 9, and 12 months. Outcomes will include headache-related disability, functional health status, patient satisfaction, appropriateness of care, and resource utilization. Data analysis will evaluate study group (intervention/control) as the primary predictor variable, and will incorporate hierarchical linear modeling techniques, given the nested nature of the data. Control variables (covariates) include site, physician, patient

<sup>&</sup>lt;sup>2</sup> 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).

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demographics, and clinical characteristics. Various outcome and process measures will be used as the dependent variable(s) in specific modeling exercises.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

### • Project Title: A TWIN STUDY OF CHRONIC FATIGUE SYNDROME IN SWEDEN

Principal Investigator & Institution: Pedersen, Nancy L.; Karolinska Institute Tomtebodavagen 11F Stockholm,

Timing: Fiscal Year 2001; Project Start 15-AUG-2001; Project End 31-JUL-2004

Summary: Despite considerable research, fundamental questions about CFS remain at best partially answered. These questions include its definition, validity, the degree to which it results from genetic versus environmental factors, the nature of the substantial comorbidity observed with other conditions, and the basis of the female preponderance. The overarching aim of this project is to shed light on a number of basic questions about CFS via a large, population-based classical twin study. First, we will collect data on approximately 32,000 adults aged 42-65 years (13,000 complete twin pairs) who are members of the population- based Swedish Twin Registry for persistent fatigue, several overlapping conditions (fibromyalgia, irritable bowel syndrome, tension headache, allergy/eczema, generalized anxiety disorder, and major depression), and a detailed medical history. Second, the medical records of all twins who appear to have CFS-like illness and a subset of those with "CFS-explained" will be requested via an efficient national retrieval system. Following expert review, these individuals will be classified in regard to the CDC CFS criteria. Obtaining these unique data will allow us to address a set of critical questions regarding CFS. First, we will estimate the prevalence of CFS and its common comorbidities (fibromyalgia, irritable bowel syndrome, tension headache, allergy/eczema, generalized anxiety disorder, and major depression) in one of the largest samples yet studied. Second, we will use a variety of multivariate techniques to derive an empirical typology of prolonged fatigue and to assess how this typology compares to the CFS definition. Third, we will quantify the genetic and environmental sources of variation for CFS and its comorbid conditions. Fourth, critically, we will examine the influence of gender on these sources of variation. Finally, we will analyze the patterns of comorbidity between CFS and fibromyalgia, irritable bowel syndrome, tension headache, allergy/eczema, generalized anxiety disorder, and major depression using multivariate twin analyses and thereby to estimate the extent of overlap between the shared and unique genetic and environmental sources of variation. In concert with other twin studies being conducted by the investigators and their collaborators, we hope to hasten progress in understanding the etiology of CFS by parallel studies in multiple populations. The current proposal has several unique aims and represents a costeffective means to extend this work in an epidemiological sample that is arguably the best twin registry in the world.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

### Project Title: ACUPUNCTURE FOR THE TREATMENT OF HEADACHE

Principal Investigator & Institution: Coeytaux, Remy R.; Family Medicine; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, Nc 27599

Timing: Fiscal Year 2002; Project Start 01-JUL-2002; Project End 30-JUN-2007

Summary: (provided by applicant): Candidate: Remy Coeytaux, M.D. is an assistant professor of Family Medicine at the University of North Carolina (UNC), a doctoral student in Epidemiology, a medical acupuncturist, and a former Robert Wood Johnson Clinical Scholar. Research career development plan: The career development plan

includes coursework, tutorials, and mentored research activities to provide the candidate with further training in clinical trial methodology, acupuncture practice and research, headache research, and academic leadership. Immediate career goals: To become a productive and independent investigator who can apply rigorous research methods to the study of acupuncture, while at the same time respecting acupuncture traditions that may contribute to clinical outcomes. Long-term career goals: To become a Professor of Family Medicine who successfully integrates clinical acupuncture with conventional medical practice and research. Research projects: Project 1 is a randomized clinical trial (N=100) to assess the efficacy of acupuncture as an adjunct to medical care for the treatment of headache. Project 2 (N=30) will test the feasibility of a novel acupuncture comparison group that may make it possible to mask acupuncturists from subjects' treatment arm allocation. These two projects will provide preliminary data and guide the design of a subsequent R-O1 application for a "triple"-blind, randomized, placebo-controlled trial of acupuncture for headache. Environment: Patients will be recruited from the UNC Headache Clinic, and the clinical trials will be conducted through the NIH-funded General Clinical Research Center at UNC. Mentorship: Mentorship will be provided by a team of senior-level researchers, including a leader in education of complementary and alternative medicine (Dr. Curtis), a highly-experienced family medicine researcher (Dr. Sloane), a leading expert in measurement development and evaluation (Dr. DeVellis), and an expert in biostatistics and clinical trials (Dr. Davis). Outside consultants who will assist with select aspects of the proposed activities include a renowned expert, teacher, and researcher of Traditional Chinese Medicine (Dr. Kaptchuk), an epidemiologist and health services researcher with extensive experience with clinical trials of acupuncture (Dr. Sherman), and a leading expert on chronic daily headache (Dr. Spierings).

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

### Project Title: ANTIBIOTIC THERAPY FOR RHEUMATOID ARTHRITIS (ATRA TRIAL)

Principal Investigator & Institution: St Clair, Eugene W.; Duke University Durham, Nc 27706

#### Timing: Fiscal Year 2001

Summary: Previous randomized, controlled clinical trials suggest that oral tetracyclines may reduce the symptoms of joint inflammation in rheumatoid arthritis (RA). This class of antibiotics has well-described antimicrobial effects as well as anti-collagenase activity. Collagenase is an enzyme that degrades cartilage and bone and is believed to be important in the pathogenesis of RA. This study evaluated the safety and potential clinical efficacy of I.V. doxycycline therapy in 31 patients with RA and explored whether any improvements in arthritis from the doxycycline were due to its antibacterial actions or ability to reduce the activity of collagenase. The three objectives of this study were: 1) To determine the feasibility, safety, and potential clinical efficacy of I.V. doxycycline therapy in RA and explore whether this agent ameliorates clinical manifestations of this disease by suppressing bacterial infection or matrix metalloproteinases (MMP) activity; 2) To determine whether daily and weekly treatment with I.V. doxycycline can reduce urinary excretion of collagen crosslinks in patients with RA and potentially retard joint damage; and 3) To explore the potential effects of daily and weekly I.V. doxcycline therapy on biochemical markers of cartilage proteoglycan degradation; and 4) to determine whether IV doxycycline can reduce expression of nitric oxide synthase type 2 expressed by circulatory monocytes. Patients were randomized into 3 groups: Group I received I.V. doxycycline and oral placebo, Group II will received I.V. placebo and oral

azithromycin, and Group III received I.V. and oral placebo. The I.V. therapy was delivered through a peripheral long-line catheter. The initial treatment phase consisted of daily infusions and oral therapy for 21 days. The second treatment phase consisted of weekly infusions administered from week 4 through 11. Results: The study is closed and a Final Report was submitted to the NIH on December 29, 1998. Thirty-one patients were enrolled between April of 1995 and February 1998. The study population included various ethnic backgrounds, such as African- American, Caucasian, and Native American and was predominantly female (24/7). Only 4 patients withdrew from the trial before the day 112 visit. Three patients discontinued the study drug after day 28 because of worsening arthritis and one patient withdrew at day 56 when she was diagnosed with breast cancer. Thirteen (42%) of the patients experienced at least one infusion-related event during the trial. These events included catheter site tenderness/pain/redness, symptoms of burning during the infusion, site-related skin rash from adhesive tape, catheter infiltration, signs of localized infection at the catheter site, clotting of the catheter or line, and thrombophlebitis. None of these events were classified as serious. Most of the patients experienced at least 1 adverse event, which were most commonly gastrointestinal or neurologic in origin. The most frequent adverse events apart from the infusion-related complications included headache (8 patients), abdominal pain (6 patients), fatigue (6 patients), nausea/vomiting (5 patients, vaginitis (5 patients), loose stools/diarrhea 93 patients), dizziness/lightheadedness (3 patients), and decreased appetite (3 patients). The results of the present study do not provide evidence that i.v. doxycycline therapy reduces the signs or symptoms of RA. These data must be interpreted with caution because the study was not designed to provide adequate statistical power to answer this question. The present study does show that this treatment approach is feasible and does not cause unacceptable toxicities. However, no significant differences were noted among treatment groups in the primary endpoints. The tender joint count dropped only slightly in all of the 3 treatment groups. This result is compatible with little or no immediate clinical effect from the 3 weeks of i.v. doxycycline therapy. Significance: There are no future plans since doxycycline did not improve the primary endpoints.

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### Project Title: AUTONOMIC STRESS REACTIVITY IN FIBROMYALGIA

Principal Investigator & Institution: Okifuji, Akiko; Associate Professor; Anesthesiology; University of Utah 200 S University St Salt Lake City, Ut 84112

Timing: Fiscal Year 2001; Project Start 01-JUL-1999; Project End 30-JUN-2004

Summary: This is an R21 application proposing to conduct a preliminary study on the relationship between autonomic stress-reactivity and pain sensitivity in patients with fibromyalgia syndrome (FMS). Although the exact pathphysiologic mechanisms of FMS are yet to be determined, FMS is generally considered as a disorder involving dysregulated central pain modulation. In addition, FMS seems to be associated with dysfunctional stress adaptation. Many FMS patients report that stress exacerbates their pain and symptoms. Research has suggested that autonomic dysregulation exists in FMS. FMS patients tend to exhibited blunted autonomic reactivity to noise, cold, and physical stressors. Research in cardiovascular and **headache** disorders, as well as animal/human laboratory studies, have demonstrated the antinociceptive effects of increased arousal, particularly baroreflex and occulosympathetic reactivity. These previous reports suggest that dysregulated autonomic functions in response to stressors play an important role in elevated pain sensitivity and other FMS symptoms. In the proposed study, we hypothesize that 1) FMS is associated with blunted sympathetic

reactivity, 2) FMS is related to increased susceptibility to develop orthostatic intolerance, and 3) stress-induced analgesics are minimized in FMS. 30 FMS patients, 30 patients with temporomandibular disorder (TMD: localized pain control), and pain-free healthy subjects will undergo various stress tasks, orthostatic torelance test, and pain sensitivity test while blood pressure and pupil size are continuously measured. The levels of stress associated with tasks are relatively moderate (mental arithmetic, discussion of stressful experience), thereby allowing us to determine the importance of daily stressors patients report as an aggravating factor. Results from this study thus should provide initial evidence regarding the effects of stress-induced dysautonomia in FMS symptoms. Furthermore, the results of the study may provide an important avenue for improving those symptoms secondary to autonomic dysfunction.

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### Project Title: BIOMARKER FOR SUBARACHNOID HEMORRHAGE

Principal Investigator & Institution: Zemlan, Frank P.; Professor; Phase 2 Discovery, Inc. 3130 Highland Ave, 3Rd Fl Cincinnati, Oh 45219

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

Summary: (provided by applicant): The objective of this Phase I application is to develop a new quantitative clinical biomarker for subarachnoid hemorrhage (SAH). Acute headache is initially screened for SAH by computed tomography (CT). CTnegative patients suspected of SAH are then screened for cerebrspinal fluid (CSF) xanthochromia, which has documented limitations and is not FDA-approved. The present application proposes to develop a new biomarker, cleaved MAP-tau (C-tau). The proposed biomarker should demonstrate increased sensitivity and specificity, as well as, improving point of care treatment by using immunocard technology. We have developed a sandwich ELISA that specifically quantifies this neuronally localized protein, C-tau, that is released from damaged neurons. Employing our C-tau ELISA, we demonstrate in preliminary studies that CSF C-tau levels are elevated 1,000 fold in SAH patients compared to neurologic controls. Our Specific Aims are: Specific Aim 1: Determine if CSF C-tau levels are significantly elevated in CT-negative acute headache patients with SAH compared patients without SAH determined at three month follow up (N=150). Specific Aim 2: Determine if differences in CSF C-tau level between SAH(+) and SAH(-) patients are time dependent (Specific Aim 1).

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### • Project Title: BRAIN STEM MECHANISMS MEDIATING THE NOCICEPTIVE PRESSOR RESPONSE

Principal Investigator & Institution: Felder, Robert B.; Professor; University of Iowa Iowa City, Ia 52242

Timing: Fiscal Year 2001; Project Start 01-JAN-2001; Project End 31-DEC-2001

Summary: The goal of this proposal is to determine the role of the lateral parabrachial nucleus (LPBN) in mediating the cardiovascular responses to pain. Noxious stimulation typically elicits increases in arterial blood pressure and heart rate. These responses are mediated by nociceptive and cardiovascular centers in the brain stem. Recent anatomical and electrophysiological studies point to the LPBN as the major projection site for nociceptive inputs from lamina I and lamina II neurons in the spinal cord and the spinal trigeminal sensory nucleus in medulla. Moreover calcitonin gene-related peptide (CGRP) and substance P (SP), neuropeptides prominently involved in sensory afferent and nociceptive pathways, are present in LPBN and have been implicated in

ascending pain pathways. These studies will use single cell electrophysiological recording techniques, recordings of arterial pressure, heart rate and sympathetic nerve activity, and functional neuroanatomy (c-fos) to determine the role of the LPBN in mediating the nociceptive pressor response by stimulating the trigeminal afferent system which has a discrete termination site in caudal medulla and well defined projection pathways to LPBN. The influence of the solitary tract nucleus (NTS) will also be examined, though existing data suggest a secondary role for NTS in this process. Finally, the interactions of baroreceptor afferent signals with noxious inputs will be determined at LPBN and at the rostral ventrolateral medulla (RVLM), the medullary sympathetic outflow site for the pressor response. The trigeminal afferent system mediates a number of important clinical pain syndromes, including migraine headache, the headache of arachnoid hemorrhage, trigeminal neuralgia, temporal mandibular joint pain and corneal and oral cavity pain. Thus, a better understanding of the central neural mechanisms mediating cardiovascular responses to noxious trigeminal stimulation may ultimately lead to new management strategies for patients with these clinical syndromes. In addition, these findings will contribute to the basic understanding of the central link between nociceptive afferent signals and cardiovascular regulation.

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### • Project Title: CALCIUM SIGNALLING AMONG NON-NEURONAL BRAIN CELLS

Principal Investigator & Institution: Nedergaard, Maiken; Professor; Cell Biology and Anatomy; New York Medical College Valhalla, Ny 10595

Timing: Fiscal Year 2001; Project Start 01-AUG-2001; Project End 31-JUL-2005

Summary: In previous studies, we have reported that calcium waves among gap junction-coupled glia may form the cellular substrate for spreading depression in vivo. Recently, we have noted that calcium waves initiated in astrocytes in slices can propagate to brain endothelial and meningeal cells; all of these cell types express connexin43, which may allow their mutual heterotypic syncytial interaction through homotypic gap junctions. On this basis, we propose to test the hypothesis that astrocytic calcium waves may thereby invade the brain by propagating along the capillary vasculature, as well as through the astrocytic syncytium. These experiments will test the possibility that endothelial calcium waves may follow the venular endothelium to invade the meningeal vasculature, thereby recruiting both meningeal cells and trigeminal sensory afferents. This proposed pathway, by bypassing and traversing the restrictive barrier of the pia limitans, would permit the recruitment of both the meningeal vasculature and its trigeminal sensory afferents into parenchymal waves of spreading depression. We propose here that this scenario might operationally model the initiation of migraine **headache** in adults. In parallel experiments, we will also follow-up our recent observation of a steroid-induced accentuation of astrocytic calcium signaling, by asking whether calcium signaling among non-neuronal brain cell types may be modulated by gonadal steroids. In particular, we seek to determine whether the cyclical female hormones estrogen and progesterone potentiate signaling from astrocytes to endothelial cells, and if so, whether the likelihood of meningovascular recruitment into a parenchymal calcium wave is thereby increased. This pathway might account for much of the symptomatology of migraine headache, while steroidal accentuation of calcium signaling might account for the cyclicity of migraine occurrence. The longdistance multicellular calcium signaling pathway that we propose, and its attendant hormonal regulation, suggests immediately testable strategies for its abrogation.

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### Project Title: CENTRAL NERVOUS SYSTEM INVASION IN EARLY LYME DISEASE

Principal Investigator & Institution: Coyle, Patricia K.; Associate Professor; State University New York Stony Brook Stony Brook, Ny 11794

Timing: Fiscal Year 2001

Summary: Lyme disease, due to the spirochete Borrelia burgdorferi, is a major emerging infection in our country. Neurologic involvement has become the significant morbidity of this infection, but has not been well studied. Effective public health poll is being hampered by lack off basic information on clinical and laboratory features and pathogenetic mechanisms of Lyme disease. The objective of this proposal is to identify the frequency, clinical correlate and outcome of central nervous system (CNS) infection in early Lyme disease. This study will focus on 3 adult case groups (N=100) with newly acquired infection: 1) single lesion erythema migrans (EM) (N=25); 2) multifocal EM (N=25); 3) neurologic Lyme disease (N=50). All eligible patient will meet Centers for Disease Control and Prevention diagnostic criteria for Lyme disease. After an initial comprehensive evaluation (self report forms to assess clinical symptoms, psychosocial and psychiatric measures, and health outcome; skin, blood and cerebrospinal fluid (CSF) studies; cognitive assessment) subjects will receive standard antibiotic treatment, and then be followed prospectively for 18 months. Comparison groups will be healthy subjects (N=1 00) frequency matched to cases on age, education and gender; and subjects with other neurologic diseases (N=50). Specific Aim 1: To determine the frequency of CNS invasion in early local and disseminated Lyme disease (invasion will be defined by positive CSF culture, Borrelial antigen, Borrelial DNA, or intrathecal Borrelial antibodies); to document neurologic complaints and health function status of early infection patients. Hypothesis: CNS invasion by B. burgdorferi is common during early infection. Corollary: neurologic complaints are frequent in early Lyme disease. Corollary: in this population new onset of headache is a clinical marker of CNS invasion, while CSF IgM reactivity to B.burgdorferi is an immune marker of CNS invasion. Specific Aim 2: To examine the outcome of neurologic involvement in, early Lyme disease. Hypothesis: Following infection, patients with persistent CSF abnormalities (defined as CNS invasion markers; Borrelial immune complexes; or abnormal cell count or protein) will be symptomatic. Corollary: clearance of CSF is associated with clinical improvement. Specific Aim 3: To determine the proportion of early Lyme disease patients who develop late encephalopathy. Question: what proportion of early Lyme patients will develop persistent neurobehavioral dysfunction in domains of attention and memory? This proposal will help characterize the neurologic aspects of early Lyme disease, will aid in diagnosis and management, and will help guide the formulation of a rational and cost effective health care program for Lyme disease.

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#### Project Title: CHRONIC PAIN MANAGEMENT IN PRIMARY CARE

Principal Investigator & Institution: Von Korff, Michael R.; Senior Investigator; University of Washington Seattle, Wa 98195

Timing: Fiscal Year 2001; Project Start 01-JAN-1989; Project End 31-AUG-2004

Summary: This research seeks a more effective and cost-effective integration of medical care and self-care for chronic and recurrent pain in pr5imary care settings. Aim 1: Identify improved methods for analysis of automated health care and medicine use data for TMD pain, **headache** and back pain patients. Identify potentially modifiable

determinants of long-term frequent use of health care and pain medications for these conditions. Study One: We will study determinants of health care and prescription medicine use for pain over a five-year time span. {{Methods for analysis of automated health care and medicine use data will be assessed to test more powerful and informative approaches. Using improved analytic methods,}} we will assess the ability of patient variables to predict and explain frequent use of health care, opioid medications and sedative- hypnotic medications for patients with TMD (n=391), back pain (n=833) and headache (n=869) over a five year time-span. Aim 2: Evaluate the effectiveness of Self-Care Group interventions guided by a stepped care model. Study Two: Data from two randomized controlled trials of Self- Care Groups (SCG) initiated in 1996-98) as part of the current Program Project will be used to identify factors influencing the long-term effectiveness of SCG (participation, baseline severity, self-care orientation, prognostic variables). Study Three: A new randomized controlled trial will evaluate Self-Care Groups fully integrated into primary care. This trial will evaluate the initial benefits and the long-term effectiveness of Self-Care Groups among actively recruited back pain patients (n=250). The intervention will target patients with enduring activity limitations and higher use of health care for back pain {{Patients with continuing activity limitations will receive more intensive intervention according to a stepped care protocol.}} Patients will be followed-up 2, 6, 12 and {{24}} months after randomization. The primary outcome will be activity limitations (Roland Disability Score with added items concerning occupational role disability). Aim 3: Assess the impact of Self-Care Groups (SCG) on long-term health care and prescription medication use. Determine the effect of SCG on health care costs. Study Four: Using automated health care and medicine use data and improved analytic methods, we will investigate the long-term effects of SCG on: (1) use of health care; (2) use of prescription pain medications; and (3) health care costs for back pain (total n from three SCG trials=731). Since the SCG interventions have been shown to reduce worry, enhance confidence in self-care, and reduce activity limitations, this research will provide an experimental test of whether modifying these factors reduces subsequent use of health care.

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### Project Title: CLINICAL AND MOLECULAR PATHOPHYSIOLOGY OF HEADACHE

Principal Investigator & Institution: Harrington, Michael G.; Professor/Research Director; Huntington Medical Research Institutes 734 Fairmount Ave Pasadena, Ca 91105

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

Summary: (provided by applicant): The long-term objective of our research is to discover what clinical and molecular changes occur before, during and after severe **headaches.** Our hypothesis is that the myriad **headache** triggers and behavioral expressions are mediated through interacting molecular pathways that may be studied by temporal, compositional analysis of accessible body fluids, in particular cerebrospinal fluid (CSF). Preliminary results have revealed many ictal changes in proteins, lipids and elements that reflect these migraine 'gateway' pathways, the magnitude of which reflect the clinical severity of the migraine ictus, suggesting a corresponding 'molecular ictus'. We propose to further dissect this clinical and molecular ictus by the analysis of CSF from migraineurs in **headache** and non-headache states, episodic tension **headache** sufferers and 'controls' who do not suffer from **headaches**. We will test the role of protein, lipid and elemental changes in **headache** by defining their molecular composition by 2D gel electrophoresis, liquid chromatography and mass spectrometry

in temporally spaced collections from clinically well defined participants. Delineation of these compositional differences should extend our pathophysiological understanding beyond the current theories, yield useful biomarkers and lead to more knowledge-based remedies or interventions.

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#### Project Title: COCHLEAR BLOOD FLOW AND NEUROPEPTIDES

Principal Investigator & Institution: Nuttall, Alfred L.; Professor; Otolaryngology Head & Neck Surgery; Oregon Health & Science University Portland, or 972393098

Timing: Fiscal Year 2001; Project Start 30-SEP-1995; Project End 31-JUL-2003

Summary: The migraine related inner ear symptoms for phonopobia, tinnitus, hearing fluctuation, hearing loss, and increased noise sensitivity provide evidence for a possible neurological substrate connecting basilar artery migraine and cochlear pathophysiological mechanisms. Recently we have identified a previously unreported sensory innervation of the cochlear blood vessels originating from the trigeminal ganglia. We have shown that this sensory innervation has a significant effect on cochlear blood flow (CBF) in both normal and pathological conditions (e.g., in the animal model of endolymphatic hydrops, one of the symptoms of Meniere's disease). This proposal seeks to further define the anatomical basis and mechanisms of the trigemino-sensory network around the vertebrovasilar and cochlear vascular system. The proposal offers the hypothesis that the trigemino-sensory system and its related neuropeptide system are important factors contributing to basilar migraine and vascular homeostasis of the cochlea. The study has three specific aims. Aim 1. To establish if there is a physiological basis for the cochlear symptoms in basilar artery migraine headache. Positive results will confirm a common functional basis for basilar migraine and cochlear symptoms, the basis could be neurogenic inflammation. Aim 2. To demonstrate if vanilloid receptor (VR1) and substance P (SP) are co-localized around cochlear blood vessels, the basilar artery and its related branches. Positive immunocytochemical results will demonstrate: (a) network of the VR1 and (b) SP co-labeled primary sensory neurons around the basilar artery; anterior inferior cerebellar artery (AICA), spiral modiolar artery (SMA) and radial artery; (c), Capsaicin will cause a significant reduction in the density of labeled sensory fibers. Aim 3. To determine the vasoregulatory disturbance of the trigemino-sensory neurons in endolymphatic hydrops. In this study positive results will demonstrate that endolymphatic hydrops causes a reduction in the stimulated trigeminal ganglion induced CBF change. The studies of the proposal will help clarify how trigemino-sensory neurons regulate the vertebro-basilar vascular system and cochlear fluid balance under normal and pathological conditions.

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### Project Title: COMPARISON OF COGNITIVE TREATMENTS FOR HEADACHE PAIN

Principal Investigator & Institution: Thorn, Beverly E.; Psychology; University of Alabama in Tuscaloosa Tuscaloosa, Al 35487

Timing: Fiscal Year 2001; Project Start 20-SEP-2001; Project End 19-SEP-2004

Summary: APPLICANT?S Cognitive-behavioral interventions are an effective component of multidisciplinary treatment for patients with pain problems. The critical components for treatment success are not known, nor is it understood why CBT works better for some patients than for others. Very few studies have evaluated the utility of specific components of CBT for pain, and the comparison of cognitive components of

CBT is particularly lacking. The first aim of this study is to conduct a randomized control comparison of two cognitive-behavioral interventions for headache pain to a delayed treatment control group. The two cognitive interventions employed will be treatment focused on the reduction of pain-specific dysfunctional cognitions and treatment focused on teaching cognitive coping strategies Participants in this study will be referred by local neurologists and will meet diagnostic criteria for migraine and/or tension-type headache. Comprehensive assessments will be conducted before treatment and following 8 weeks of treatment (primary endpoint). Primary outcome measures will include: self-reported pain intensity and frequency of headaches and pain medication use. Secondary outcome variables will include measures of depression, anxiety, dysfunctional thinking, catastrophizing, cognitive coping and self-efficacy. It is predicted that patients who receive treatment will show significant treatment gains compared to the delayed treatment group. However it is expected that cognitive restructuring will result in greater treatment gains than coping skills training. The second aim of the study is to examine the effect of catastrophizing, a specific individual variable that has been shown to predict pain treatment success. Individuals who score high on measures of catastrophizing display poorer physical and psychosocial functioning. These individuals also evidence poorer response to treatment. It is hypothesized that baseline catastrophizing scores will be a predictor of treatment success. Participants who score higher on a measure of catastrophizing will show less improvement than individuals who score lower on this measure. However, catastrophizers will show greater relative improvement with cognitive restructuring than with coping skills training. Future research will consider the potential effects of combining these treatments as well as the impact of order of component presentation.

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### Project Title: CORTICAL INHIBITION DURING VISUAL PERCEPTION IN MIGRAINE

Principal Investigator & Institution: Cao, Yue; Associate Professor; Radiology; Michigan State University 301 Administration Bldg East Lansing, Mi 48824

Timing: Fiscal Year 2001; Project Start 05-APR-2001; Project End 30-MAR-2003

Summary: Migraine is a common neurological disorder, affecting nearly 12% of the populations in the US with a high incidence in females. Migraine headache pain can lost hours to days, and causes considerable discomfort, disability and days lost from work Visual symptoms are profound in migraine. Visual aura can occur prior to the onset of migraine pain. Photophobia and vision blurring are associated with most migraine attacks, with or without aura. A neuronal hyperexcitability, particularly in the visual cortex, is a generalized hypothesis in migraine pathophysiology. One mechanism responsible for cortical hyperexcitability might be deficient inhibition by g-aminobutyric acid (GABA)ergic interneurons. In the primary visual cortex, GABAergic neurons form a diffuse horizontal network in lamina IV and are very likely to be selectively vulnerable to hypoperfusion/hypoxia occurring during migraine attack. In response to PA-98-050, the applicants propose to explore an innovative approach to study visual cortical excitability in migraineuers with visual aura by examining excitatory and inhibitory interaction during visual perception. Specifically, they will develop robust psychophysical methods to determine the extent of visual cortical inhibition, both in migraine subjects and non-headache controls, during visual masking. They will develop fMRI methods to determine cortical response to the un-masked (non-inhibited) and masked (inhibited) visual targets in non-headache and migraine individuals. The hypotheses are: (1) The invisible (inhibited) visual target in non-headache controls is visible (non-inhibited) or partially visible (partially non-inhibited) to migraineurs with visual aura in whom visual cortical inhibition is deficient; (2) The non-inhibited visual target in migraineurs induces a neuronal response in primary visual cortex and the inhibited visual target in non-headache controls does not evoke a neuronal response. In order to test the hypotheses, they will develop new fMRI methodologies in image cortical responses to the visual stimuli that are temporally brief (20ms to 100ms), and dimensionally small (subtending 0.5 to 4 degrees of visual angles). There are parameters associated with visual masking. Successful developing these new methodologies is not only crucial for the proposed study, but also extremely valuable for other brain research. Furthermore, the scientific concept proposed here may lead to an innovative approach to investigate visual function/dysfunction in migraine, and may provide a new insight into migraine pathophysiology.

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### Project Title: CORTICOTROPIN-RELEASING FACTOR ROLE IN CYCLIC VOMITING

Principal Investigator & Institution: Li, B U.; Children's Memorial Hospital (Chicago) Chicago, Il 606143394

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

Summary: (provided by applicant): Cyclic vomiting syndrome (CVS) is the most severe recurrent vomiting disorder in humans and is more prevalent than previously appreciated (1 in 50 school-aged children). Although the pathogenesis remains unknown, corticotropin-releasing factor (CRF) is a tenable candidate brain-gut neuroendocrine mediator of vomiting in CVS. CRF has a well-established role in inducing gastric stasis and vomiting in animals and its resulting behavioral, autonomic, endocrine effects resemble those clinical features seen in CVS. The model of CRFinduced emeses may explain the antiemetic utility of dexamethasone during chemotherapy-induced vomiting and migraine headaches. We hypothesize that systemic CRF levels and hypothalamic-pituitary-ad renal (HPA) axis activity are heightened during episodes of CVS and migraine headache especially in those who experience concomitant nausea and vomiting. To provide direct clinical evidence of involvement of CRF pathways in CVS and migraine, we will examine CRF and HPA axis activation (ACTH, cortisol, catecholamines) in subjects with CVS, migraine headaches and controls under three conditions including: 1) when well (i.e. in between episodes), 2) during acute episodes of cyclic vomiting or migraine headaches treated with a saline placebo, and, 3) during acute episodes of cyclic vomiting or migraine headaches in which CRF is treated by dexamethasone. Under each condition, we will establish the diurnal variation of CRF and HPA axis activity and compare them to pediatric controls, both healthy and with non-CVS vomiting (gastroenteritis). In a randomized, double blind, cross-over design, we will examine the effect of dexamethasone on CRF and HPA axis activity, objective signs and subjective GI and migraine headache symptoms. CVS and migraine headaches may ultimately both be disorders involving dysregulation of CRF pathways.

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### Project Title: DEVELOPMENT OF A LIVE ORAL CHOLERA VACCINE

Principal Investigator & Institution: Kaper, James B.; Professor; Microbiology and Immunology; University of Maryland Balt Prof School Baltimore, Md 21201

Timing: Fiscal Year 2001; Project Start 01-JAN-1983; Project End 31-JAN-2006

Summary: (Adapted from the Applicant's Abstract): An ideal vaccine for the prevention of cholera is not yet available. Previous work in this project has resulted in the development of an attenuated live oral cholera vaccine, V. cholerae CVD 103-HgR. This vaccine confers strong protective immunity against experimental challenge with virulent V. cholerae O1 after a single dose. Although this vaccine is highly protective in North American volunteers and has been licensed in several highly developed countries for protection of travelers to cholera endemic countries, a recent field trial of this vaccine in Indonesia failed to show efficacy. The development of attenuated cholera vaccines has been plagued by the fact that V. cholerae strains deleted of the ctx genes encoding cholera toxin can still produce varying amounts of diarrhea and non-diarrheal symptoms such as headache, fever, abdominal cramps, and malaise in many individuals. Such symptoms are not seen with CVD 103-HgR, in all probability because this strain colonizes the human intestine at greatly reduced levels compared to the reactogenic, avidly colonizing ctx-negative strains. Although the reduced colonization of CVD 103-HgR was still sufficient to engender a protective immune response in North American volunteers whose small bowel intestinal flora is relatively sparse, it was not sufficient to induce a protective immune response in a cholera-endemic population with a heavy burden of small bowel intestinal flora which would compete against a live oral vaccine strain. The ability to construct a better-colonizing strain is hampered by the uncertainty as to what bacterial factor is responsible for the reactogenicity. Thus, the next period of support for this project will focus on characterizing the response of epithelial cells to adherent V. cholerae, establishing the role in reactogenicity of various cytolysins, proteases, other degradative enzymes, and other potential toxins revealed by the recently completed genome sequence of V. cholerae, and determining the V. cholerae genes that are specifically expressed during the course of human infection. These studies will use the broadest possible range of models to study host-pathogen interactions, including intestinal epithelial cell lines, freshly harvested human intestinal tissue, animal models, and human volunteer studies.

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### Project Title: DRUG AND NON-DRUG TREATMENT OF SEVERE MIGRAINES

Principal Investigator & Institution: Holroyd, Kenneth A.; Professor; Psychology; Ohio University Athens Athens, Oh 45701

Timing: Fiscal Year 2001; Project Start 30-SEP-1994; Project End 31-AUG-2005

Summary: (Adapted from investigator's abstract) The proposed study evaluates the effectiveness of preventive drug (beta-blocker) therapy and non-drug (behavioral migraine management) therapies for frequent migraine, both separately and when combined. The specific aims are to: (1) Evaluate the separate and combined effects of Preventive Drug Therapy and limited-contact Behavioral Migraine Management, with reference to Placebo in a (n=220) prospective outcome study; (2) Evaluate the effectiveness of these treatments of individuals with frequent (4-15 migraine days/month) disabling (above the population median in disability) migraine; (3) Evaluate the effects of these treatments on multiple outcome measures, including migraine activity, disability, quality of life, psychological symptoms and beliefs about migraines; (4) Evaluate the effects of these treatments on the use, effectiveness and cost of acute (5HT1 antagonist) therapy; (5) Evaluate intermediate (6 months) and long-term (1-year) treatment effects. Examine psychological variables hypothesized to be associated with the maintenance of treatment effects. Two hundred twenty patients meeting International Headache Society (Olesen, 1988) diagnostic criteria for migraine (w or w/o aura) and who experience frequent (4 to 15 migraine/days month) and disabling (above the median of migraine sufferers in disability) migraine will participate in the following three phases of this study: (1) pretreatment evaluation that includes structured diagnostic and psychosocial interview, neurological evaluation, psychosocial testing and at least 5 weeks baseline daily monitoring of migraine activity, migrainerelated disability and medication use; (2) a three-month treatment (administration/dose adjustment) phase where standard acute therapy plus one of the following four preventive therapies are administered in a 2 x 2 factorial design: Preventive Drug Therapy with beta-blockers, or Preventive Drug Therapy with placebo, or Behavioral Migraine Management Therapy + beta blockers, or Behavioral Migraine Management + placebo and, (3) a 12-month long evaluation phase where continuing care is provided and treatment efficacy is assessed at 1-month, 6-months and 12-months follow follow-up evaluations (with neurological & psychosocial evaluations and 5 additional weeks of daily **headache**, disability and medication recordings).

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

#### Project Title: ELECTRONIC HEADACHE DIARY

Principal Investigator & Institution: Johannes, Catherine B.; Director; New England Research Institutes, Inc. 9 Galen St Watertown, Ma 02472

Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2003

Summary: (provided by applicant): At least 45 million Americans suffer from severe headaches annually that seriously impact their work and daily life. Headache diaries are an integral part of **headache** management, assisting patients and care providers with diagnosis, identification of triggers, and assessment of therapeutic regimens. Current paper diaries are non-standardized, cumbersome, and difficult to analyze and interpret. The purpose of this Phase II proposal is to develop and evaluate software for a standardized, customizable electronic headache diary to collect daily information about headache attacks and related events in clinical and research populations. In Phase I, prototype software was developed to capture detailed information on daily headaches and tested on headache clinic patients. In Phase II the software will be expanded to include information on possible triggers and more detailed medication data. Testing will be performed on potential end users: headache sufferers and health care providers. Features will include data entry by screen tap, reminders to enter and transmit data, daily health tips, encrypted wireless data transmission, and on-line clinical data summaries. The software, AheadPC, will be designed for mobile computing devices that are convenient and easy to use, and through innovative Internet server technology, will provide interactive on-line clinical data summaries to headache patients and care providers. PROPOSED COMMERCIAL APPLICATION: Annual direct medical costs for migraine care are estimated at \$1 billion per year in the Unites States (Hu et al., 1999). Data collected prospectively about headaches is critical to diagnosing and managing patients. AheadPC aims to provide a standard, clinically valid, method of collecting headache data on a handheld computer with results viewable by ID to both patients and clinicians via the World Wide Web. With an estimated 45 million Americans experiencing severe headaches per year, the market for AheadPC is very strong in a variety of areas, including use by individuals, practitioners, and researchers.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

### • Project Title: ENZYME AUGMENTATION THERAPY OF GAUCHER DISEASE

Principal Investigator & Institution: Grabowski, Gregory A.; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

#### Timing: Fiscal Year 2001

Summary: The objective of this ongoing study is to evaluate and delineate the long-term therapeutic effects of enzyme replacement therapy in Gaucher disease in affected children and adults. In addition, efforts are directed to identifying and delineating the causes for and treatment of adverse events related to enzyme therapy, as well as determining the effective dose in individual patients. To date, we have enrolled over forty patients in this protocol from the Cincinnati greater metropolitan area and from around the world. We have established normative data for the expected responses for patients during the first six, twelve and twenty-four months of therapy using either Ceredase (alglucerase for injection from placenta) or Cerezyme (imiglucerase for injection from recombinant sources), and have found that the responses are no different in either treatment group. The same degree of variability, which is very high, is observed with both of the drugs and we have found no specific correlation with age of onset or initiation of therapy, genotype of the individual patients, ethnic extraction, nor initial severity of disease. In general, the hepatic and splenic volumes decrease to about twenty to forty percent of initial volume by two years, the hematologic abnormalities including anemia and thrombocytopenia diminish and become normalized within approximately two to three years, and, in children with growth retardation, normal growth patterns are reestablished within two years. Documentation of improvement in architectural bone disease has been slow and unconvincing. Indeed, based on this result, we have initiated a new protocol that evaluates the effectiveness of alendronate in combination with enzyme therapy on the architectural bone disease in osteopenia of Gaucher disease. Approximately three to five percent of our patients develop minor adverse events, including hives, pruritis, erythema, and headache during or shortly following the infusion. These are managed by decreasing infusion rates and/or pretreatment with antihistamine. We have had no anaphylactic or anaphylactoid reactions. Of the fifteen percent of treated patients that develop antibodies during the course of therapy, two were found to have neutralizing antibodies that altered their responsiveness to enzyme therapy. In both cases, poor to absent response to enzyme infusions was noted and this led to the detection of the neutralizing antibodies. In one patient, a very high dose cytoxin protocol was used to induce tolerance. After two and a half years of high dose therapy, she has tolerized with the absence of both antibodies and neutralizing activity. Ongoing studies are directed to defining the time for tolerization in all patients who develop antibodies; currently this appears to be about twenty-two to twenty-four months. In addition, ongoing studies are directed to defining the parameters that account for the massive variability and response to enzyme therapy in affected patients.

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### • Project Title: EXPLORATORY PROGRAM GRANT FOR FRONTIER MEDICINE

Principal Investigator & Institution: Prestwood, Karen M.; Assistant Professor and Associate Direct; Medicine; University of Connecticut Sch of Med/Dnt Bb20, Mc 2806 Farmington, Ct 060302806

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

Summary: (provided by the applicant): In the United States, the use of complementary and alternative medicine (CAM) increased by approximately 25% between 1990 and 1997. The number of visits to CAM practitioners was 629 million and exceeded visits to primary care physicians by about 250 million in 1997. In spite of the extensive use of CAM in the US and internationally, we know little about the safety and efficacy, mechanism of action and longer-term outcomes of many popular modalities. Energy

medicine modalities, including therapeutic touch, healing touch and reiki, are commonly utilized for conditions ranging from headache to cancer yet our understanding of the human energy field and how it may be used in healing is limited. Although many of these therapies have been used for hundreds or even thousands of years, the current medical and scientific environment demands that we begin to apply rigorous standards to the study of this field. The Exploratory Center for Frontier Medicine at the University of Connecticut Health Center (UCHC), in collaboration with the University of Iowa, will focus on biofield/energy healing, specifically therapeutic touch and healing touch. We have chosen our major projects based on the research strengths of the principal investigators and designed projects in close collaboration with experienced practitioners in energy medicine. We have created a plan for collaboration between projects and between institutions which we believe will provide the infrastructure to 'nurture and advance this field of biomedical science'. The administrative core of the Center will provide the scientific and educational infrastructure for investigators in frontier medicine. The core will take advantage of the rich academic environments at the University of Connecticut and Iowa in order to provide an infrastructure in which to evaluate the effects of therapeutic and healing touch on several human diseases and processes. The four projects include basic and clinical science. The studies are: Project #1 (Dr. Karen Prestwood) The effect of therapeutic touch on bone metabolism in postmenopausal women after wrist fracture; Project #2 (Dr. Gloria Gronowicz) The effect of therapeutic touch on bone formation in vitro; Project #3 (Dr. Theresa Smith) The effect of therapeutic touch on human fibroblast biology; and Project #4 (Dr. Susan Lutgendorf) Healing touch in advanced cervical cancer: immune effects and mechanisms.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

### • Project Title: GABAPENTIN VS ESTROGEN FOR THE TREATMENT OF HOT FLUSHES

Principal Investigator & Institution: Reddy, Sireesha; Obstetrics and Gynecology; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

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

Summary: (provided by applicant): Hot flashes and other climacteric symptoms affect 75% of postmenopausal women in the US and are associated with higher rates of depression and sleep disturbance. Although hormone replacement therapy (HRT) is highly effective in reducing hot flashes, there is concern that HRT is associated with an increased risk of thrombo-embolic events, breast cancer and ovarian cancer. In addition, it is poorly tolerated in clinical practice, with about 30% of women discontinuing therapy after a mean of 4.5 months. Many other women have a contraindication to HRT, such as a history of an estrogen-sensitive tumor, liver dysfunction, or a hypercoagulable state. Safe, effective, and well-tolerated alternative therapies for hot flashes are needed. Gabapentin is a gamma-aminobutyric acid (GABA)-analog approved in 1994 for the treatment of seizures. Since then, it has been shown that gabapentin is efficacious for numerous off-label indications such as neuropathic pain, anxiety, bipolar disorder, and migraine **headaches**. The investigators have reported that gabapentin is associated with a reduction in the frequency of hot flashes in an uncontrolled series of postmenopausal women who were taking gabapentin for other indications. The investigators also report here preliminary data from a randomized, placebo-controlled trial showing that lowdose gabapentin was associated with a greater reduction in hot flash frequency than placebo after 12 weeks of treatment. However, it is not known whether the efficacy of gabapentin in the treatment of hot flashes and other menopausal symptoms is comparable to that of estrogen, the gold standard. A randomized trial of gabapentin, estrogen and placebo is needed to inform clinicians as to whether gabapentin is an effective alternative to estrogen. The first major aim of this proposal is to assess the screening and recruitment of menopausal women into a randomized trial of gabapentin, estrogen and placebo in the treatment of climacteric symptoms. The second major aim is to obtain preliminary estimates of the frequency and severity of climacteric symptoms among women receiving gabapentin, estrogen and placebo. Pilot data from these two aims will permit estimates of sample-size requirements for a full-scale randomized trial, and of the overall feasibility and cost of such a trial.

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### • Project Title: GENETIC ANALYSIS OF MIGRAINE HEADACHE

Principal Investigator & Institution: Klassen, Arthur; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

### Timing: Fiscal Year 2001

Summary: This study will attempt to determine (i.e., map) the chromosomal location of the gene(s) responsible for the genetic susceptibility to migraine **headaches** using genetic analysis of 10-25 multi-generational families (100-300 subjects) that contain multiple members with migraine **headache**. International **Headache** Society criteria will be used to determine family members affected/unaffected by migraine. Linkage analysis will be performed by standard techniques of the core lab of Dr. Richard King on blood samples drawn from subjects.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

### • Project Title: GENOMICS OF PEDIATRIC HEADACHE DISORDERS

Principal Investigator & Institution: Hershey, Andrew D.; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

Timing: Fiscal Year 2003; Project Start 15-JUL-2003; Project End 30-JUN-2007

Summary: (provided by applicant): This project will examine gene expression in the blood of patients with migraine. We have used microarrays to show that there are unique blood genomic profiles in rats following ischemia, hemorrhage, status epilepticus, and insulin-induced hypoglycemia. Recent results in humans demonstrate that gender and age have profound effects on blood genomic expression, with genes on the Y-chromosome distinguishing male from female blood samples, and lymphocytespecific genes decreasing with older age. We have also shown a specific blood genomic profile for Neurofibromatosis type 1, an autosomal dominant disease. We postulated that migraine, a non-Mendelian, hereditary disease, will have a specific blood genomic profile. Indeed, our preliminary data demonstrate that children with both acute, episodic, migraine headaches and children with chronic daily headaches have specific blood genomic profiles that are similar to each other but different from control children with other neurological diseases or to healthy controls. This proposal is designed to confirm these initial findings, and to determine whether acute migraine and chronic daily headache patients have similar or different blood genomic profiles, and whether there is a different blood genomic profile in patients that respond to NSAIDs (nonsteroidal anti-inflammatory drugs) compared to those patients that require triptans as rescue medication. The study involves taking blood samples from patients with migraine and chronic daily headaches during the headaches and during headache free intervals (internal control), and comparing these to control patients without migraine or a family history of migraine. RNA from whole blood is isolated, labeled and applied to human oligonucleotide microarrays that survey most of the human genome. Recently developed statistical programs are used to identify potential transcripts regulated in **headache** compared to control patients. Quantitative, real time RT-PCR will be used to confirm these regulated genes in each of the comparisons. The results of this study should help in beginning to develop a molecular genomic approach for the diagnosis and treatment of different **headache** disorders.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

### • Project Title: GONADOTROPIN RELEASING HORMONE AGONISTS WITH ESTROGEN IN MIGRAINE TREATMENT

Principal Investigator & Institution: Martin, Vincent T.; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

Timing: Fiscal Year 2001

Summary: Sixty percent of women who experience migraine **headaches** self report that the **headaches** worsen with their menstrual period. The current literature suggests these **headaches** may be related to rapidly falling estrogen levels on migraine **headaches** outside of the perimenstrual period. The specific aims of this study are as follows: 1) To evaluate the effect of hormone fluctuations on the severity and disability of migraine **headaches**. 2) To determine the impact of pharmacologically reducing hormonal fluctuations, using a GnRH agonist, on **headache** severity and disability. 3) To evaluate if adding constant doses of estrogen to women on a GnRH agonist decreases **headache** severity and disability in women treated with GnRH alone compared to those treated with GnRH and the estogen therapy. 5) To evaluate cerebral blood flow velocities (BFV's) and CO2 cerebrovascular reactivity (CVR) using transcranial Doppler studies (TCD) in female migraineurs at different phases of the menstrual Cycle. 6) To study the effect of hormonal manipulation (GnRH/placebo and GnRH/estrogen groups) on BVF's and CVR as compared to baseline measures.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

### • Project Title: HSV VECTORS FOR THE DESTRUCTION OF BRAIN TUMORS

Principal Investigator & Institution: Fraser, Nigel W.; Professor; Microbiology; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

Timing: Fiscal Year 2001; Project Start 01-MAY-1998; Project End 28-FEB-2002

Summary: (Adapted from Applicant's Abstract): Malignant brain tumors, both metastatic and primary occur frequently, and only palliative therapy is available at present. CNS tumors are particularly devastating to the quality of life of patients, as they frequently result in severe and debilitating neurological complications including headache, paralysis, seizures, and impaired cognition. The applicants have performed preliminary experiments in a mouse intracranial melanoma model, that demonstrate the viability of a tumor therapy approach based on the use of replication competent neuroattenuated Herpes Simplex Virus-1 (HSV-1) mutants. The rationale for this approach is that these genetically mutant viruses cannot replicate within the generally post mitotic cells of the nervous system, yet do replicate in cancer cells, which are mitotically active. Thus, they can be used to selectively lyse cancer cells within the CNS. The applicants have developed a straightforward, reproducible, clinically relevant model in which to study brain tumor therapy. The presence, progression, or regression of tumors can be imaging, assessed by non-invasive magnetic resonance and histology, immunohistochemistry, RNA in situ hybridization, and viral titration studies allow

detailed examination of viral induced effects on tumor and brain. Outcome experiments indicate that HSV-1 mutant 1716 can slow progression of pre-formed tumors, and even lead to complete regression of tumors in some animals. No deaths or untoward effects attributable to HSV-1 have been observed. The experiments outlined in this proposal will critically examine several important aspects of the tumor-virus-host relationship that is occurring. Specifically, the applicants will i) extend their preliminary data to other promising HSV-1 mutants and examine the viral and tumor cell factors that influence therapy; ii) examine the role of primary and secondary antiviral immunity in this model; iii) explore strategies to augment the effectiveness of HSV-1 based tumor therapy by combining viral therapy with ganciclovir treatment, and engineering HSV-1 mutants that will express biological response modifiers, such as IL-2, specifically within tumor cells.

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### • Project Title: INDIVIDUAL FACTORS IN NASAL IRRITANT SENSITIVITY

Principal Investigator & Institution: Shusterman, Dennis J.; Associate Clinical Professor; Medicine; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

Timing: Fiscal Year 2001; Project Start 01-SEP-2000; Project End 31-AUG-2003

Summary: (Adapted from the Investigator's Abstract): A variety of symptoms linked to indoor air pollution, including eye, nose, and throat irritation (as well as reflex nasal congestion, rhinorrhea, and sinus headache) are either mediated (or triggered) by trigeminal chemoreception. The premise that humans exhibit significant inter-individual variation in nasal trigeminal irritant sensitivity is one that has been suggested on both clinical and epidemiologic grounds, but experimentally has been incompletely investigated. The purpose of this series of experiments is to systematically explore the influence of personal factors -including age, gender, and allergic rhinitis status- on nasal irritant sensitivity, using stratified samples of non-asthmatic subjects aged 18-69 years. Operationally, "nasal irritant sensitivity" will include both perceptual acuity (the ability of an individual to detect an irritant gas or vapor) and physiologic reactivity (the tendency of individuals to experience reflex-mediated physiologic changes when exposed to irritants). For perceptual acuity, two distinct experimental systems will be employed: detection thresholds using odorless irritant (CO2), and localization thresholds for an odorous volatile organic compound (VOC). Nasal physiologic reactivity will be studies by examining changes in nasal airway resistance (NAR) after both chemical irritant (low-level chlorine) and pharmacologic (aerosolized histamine) provocation. Finally, biochemical markers of mast cell degranulation (tryphase) and neuro-immune modulation (nerve growth factor) will be assayed in nasal lavage fluid pre- and post chemical provocation in a subset of subjects. Issues of test-retest stability and cross agent generalizability of sensory tests will be examined, as will the degree of correlation between individual perceptual acuity and physiologic reactivity. The overall goals include: 1) to better understand heterogeneity of upper airway symptom reporting in polluted environments; 2) to evaluate the relationship between functional subcomponents of "nasal irritant sensitivity"; 3) to further standardize psychophysical and provocation testing protocols for possible use in clinical and/or epidemiologic settings; and 4) to explore the pathophysiology of the nasal response to irritants, including selected interactions between the sensory and immune systems.

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### • Project Title: KOREAN ACUPUNCTURE IN CENTRAL NERVOUS SYSTEM DISORDERS

Principal Investigator & Institution: Mann, John D.; Neurology; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, Nc 27599

Timing: Fiscal Year 2003; Project Start 26-SEP-2003; Project End 31-MAR-2005

Summary: (provided by applicant): Korean acupuncture is used effectively for a variety of neurological conditions in Korea, including Parkinson's disease, stroke, pain, and bladder dysfunction. Success with this mode of therapy in the United States is documented less consistently, particularly in acute and rehabilitative stroke settings and Parkinson' s. Possible explanations for this disparity include variations in: criteria for patient selection; technique; specific outcome measures; patient beliefs; methods of reporting and other unknown factors. This NIH planning grant supports development of collaborative research efforts between investigators at Kyung Hee University in Korea and UNC - Chapel Hill for the study of Korean acupuncture in the two cultures as a way of understanding mechanisms of action and factors that optimize outcomes when applied to specific neurological conditions. The proposal will bring together investigators from the two institutions with expertise in these areas to develop ideas and pilot projects leading to more extensive research proposals. The proposal requests funding for development of parallel, interactive administrative structures to support exploration of innovative research strategies, project development and investigator training. The grant will provide funding for the development of the necessary infrastructure for effective collaboration that will lead to competitive proposals integrating animal models of human disease, clinical trials, and translational research in Korean acupuncture and neurological disorders.

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### • Project Title: MIGRAINE HEADACHE TREATMENT BY DRUG AEROSOL INHALATION

Principal Investigator & Institution: Rabinowitz, Joshua D.; Alexza Molecular Delivery Corporation 1001 E Meadow Cir Palo Alto, Ca 94303

Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-JUN-2005

Summary: (provided by applicant): Migraine is a serious condition affecting millions of Americans. Patients with migraine strongly desire more rapid **headache** relief than current medications provide. A promising approach to expediting pain relief is delivery of existing drugs to the systemic circulation more rapidly via aerosol inhalation. In Phase I of this grant, Alexza MDC demonstrated the ability to form high purity, small particle size aerosols of several leading migraine medications. In addition, we have demonstrated rapid, reliable systemic absorption and quick onset of pharmacological activity of drug delivered as such aerosols to dogs. In Phase II, we will conduct the toxicology studies required to initiate human trials of such a fast-acting, inhaled migraine medication. In addition, we will optimize the convenience and reliability of the delivery device, and produce a sufficient supply of handheld, breath-actuated delivery devices to carryout a human safety and tolerability trial. Accomplishment of the goals of Phase II will lead directly to human clinical testing of a commercially viable device that could improve the lives of millions of people every year.

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### • Project Title: MIGRAINE PATHOPHYSIOLOGY AND TREATMENT MECHANISMS

Principal Investigator & Institution: Moskowitz, Michael A.; Professor; Massachusetts General Hospital 55 Fruit St Boston, Ma 02114

Timing: Fiscal Year 2001; Project Start 05-SEP-1996; Project End 31-JUL-2006

Summary: (provided by applicant): Migraine **headache** afflicts 15-20% of the population and is a major cause of economic loss. Despite its high prevalence and serious economic consequences, its neurophysiological, metabolic and molecular basis remain poorly understood and under investigated. This application represents a joint effort by basic and clinical neuroscientists to understand the biological basis of migraine headache. Our program, comprised of three (3) multi-disciplinary projects plus Scientific and Administrative Cores, aims to achieve a greater understanding of the migraine aura and headache. One project will address the consequences of the migraine visual and somatosensory aura on metabolism and neurophysiological function. The aura, often the most troublesome, and not infrequently the only symptom of migraine, may persist and very infrequently progresses to cerebral infarct. This project will use multi-modality fMRI imaging techniques to understand whether the aura has an underlying neurophysiological and metabolic signature and whether particular sub-regions of visual cortex are unusually susceptible and serve as initiators to subsequent propagating BOLD signal changes. One project proposes experiments to better understand headache and the role of sensitization within primary afferents, trigeminal nucleus caudalis and thalamus. Functional imaging will serve as the basis for this aim as well. Because we believe that migraine is accompanied by meningeal events which lead to trigeminovascular activation and the headache, this project will address the genesis of headache and the importance of nitric oxide using intravenous infusion of the nitric oxide donor, nitroglycerin, in rats, as a novel animal model. Our preliminary data support the idea that nitroglycerin infusion promotes the upregulation of inflammatory and cytokine genes within the meninges. Studies are proposed to examine the importance of oxidative and nitrergic stress leading to iNOS induction in specific dural cell populations and the importance of transcriptional mechanisms, in the interest of migraine pathophysiology and the development of new therapies.

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### • Project Title: MOLECULAR BASIS OF HEMIPLEGIC MIGRAINE

Principal Investigator & Institution: Gardner, Kathy L.; Neurology; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

Timing: Fiscal Year 2001; Project Start 05-AUG-1997; Project End 31-MAY-2003

Summary: Dr. Kathy Gardner is a Neurologist, currently gaining clinical experience with a busy private practice-entered for a 3 year period of "pay back" time to the State of Wyoming in return for a medical education loan. Prior research and laboratory experience included successful genetic linkage study of a spinocerebellar ataxia family performed during several months of her Neurology residency at the University of Utah/Howard Hughes Medical Institute. This prompted a strong interest in further study of neurogenetics, enhanced by a long standing interest in neuromuscular disorders. During private practice time she characterized and collected DNA samples on several families with inherited neurologic disorders including a very large autosomal dominant family with hemiplegic migraine. Forty five members of this family have been ascertained, clinically examined, and blood lymphocytes transformed by the applicant. The proposed laboratory research focuses on identification of the molecular basis of

hemiplegic migraine under the guidance of Dr. Eric Hoffman. During the laboratory research, didactic classes will be pursued equivalent to those taken by PhD candidates in the Department of Molecular Genetics and Biochemistry, supplemented with medical genetics coursework through the Department of Human Genetics. To further her specialized medical training, Dr. Gardner will spend 10% of her time with a headache clinic at the University of Pittsburgh under the mentorship of the Chairman of Neurology, Dr. Roger Simon. The proposed laboratory research will include: linkage analysis of the 45 member hemiplegic migraine family using chromosome l9p. If the family shows linkage to 19p, then the critical region will be genetically defined, a physical map obtained from microsatellite STSs, and candidate and novel cDNAs investigated for mutations. If the family is not linked to 19p, then a genome wide search will be done using microsatellite markers and an "affected only" approach to minimize problems of disease penetrance. Identification of the responsible gene and gene product will possibly allow initiation of clinical trials based on pathophysiology. Learning the molecular genetic techniques necessary to accomplish these goals while continuing to work and relate these findings to clinical problems will provide a strong beginning for an academic career.

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### Project Title: MULTIPLE DOSE STUDY OF SAFETY OF ABT 627

Principal Investigator & Institution: Carducci, Michael A.; Associate Professor; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

### Timing: Fiscal Year 2001

Summary: This Phase I clinical trial to test the safety, tolerability, and pharmacokinetics of ABT-627 for patients with advanced prostate cancer (PCA) and other refractory adenocarcinomas opened to accrual in July 1997. Tumor response and changes in tumor markers are evaluated. This is a dose escalation study of ABT-627 given orally each day for 28 days, followed by a week break. If there is evidence of clinical benefit, patients may continue to receive ABT-627 therapy. Nineteen patients have been enrolled across 6 dose levels (10,20,30,45,60, 75 mg/day). The cohort (18 males, 1 female) is made up of 14 patients with PCA, 2 with renal cell cancer, 2 with colon cancer, and 1 with lung cancer. Two patients are not evaluable because of early withdrawal secondary to disease progression as evidenced by cord compression. Toxicity has been minimal, with one patient experiencing a short-lived Grade 2 headache at 20 mg/day and one other patient with a Grade 3 headache for 4-5 days. Nasal congestion is the most frequent complaint. No hematologic, hepatic, or renal toxicity has been noted in the treated patients. Early pharmacokinetics are consistent with those obtained from healthy volunteers. The agent has a half-life of nearly 25 hours. Three patients with narcotic requiring pain had improvement in their pain with either a reduction in pain ratings or a decrease in narcotic use (Dose levels 10, 20, 30 mg/day) during the study period. One patient in this small cohort had a PSA decline < 50%, with the remaining PCA patients having PSA stabilization or minor declines. Of the 19 patients, 4 remain on study, 2 were withdrawn early, 4 patients progressed after 28 days of therapy, and 9 patients received therapy on the extension trial. Accrual continues to go exceedingly well. In summary, ABT-627, an ETA endothelin-receptor antagonist, is well tolerated in patients with advanced adenocarcinoma. Early PSA responses in the patients with prostate cancer and improvement in bone pain with a concomitant decrease in narcotic use is encouraging. Phase II studies with this agent are underway at this institution and other centers nationally and internationally. This Phase I trial laid the foundation for this accelerated program of drug development.
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### • Project Title: NEUROBIOLOGY OF ANOREXIA INDUCED BY MIGRAINE PAIN

Principal Investigator & Institution: Burstein, Rami; Professor; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

Timing: Fiscal Year 2001; Project Start 01-APR-2000; Project End 31-MAR-2005

Summary: Patients who experience acute, transient or persistent pain often repor6t complete or partial loss of appetite. Despite its high prevalence, the neural basis of paininduced anorexic behavior is unknown. The premise for this proposal is the association between pain and anorexia, which is particularly striking during attacks of migraine headache. The objectives of the current proposal are to gain novel understanding of the neurobiology of anorexia induced by pain using our animal model. The specific aims in this proposal have been born out of our ongoing basic and clinical studies on the pathophysiology of migraine and how intracranial pain signals research the hypothalamus. Specific Aim 1 will determine whether stimulus of the dura, which we use as a model for intracranial pain (such as migraine), can activate neurons in brain areas that mediate anorexia. Specific Aim 2 will identify the neural pathways that transmit intracranial pain signals to hypothalamic neurons that regulate feeding behavior. Specific Aim 3 will identify the chemical phenotype of the neurons activated by dural stimulation and determine whether they express molecules (such as CCK and leptin) that were shown recently to suppress appetite and used clinically to fight obesity. Specific Aim 4a will determine whether dural stimulation can suppress feeding behavior in our animal model and whether it resembles the suppression of feeding behavior during migraine attack in human subjects. Specific aim 4b will test our working hypothesis that the suppression of feeding behavior by intracranial pain is mediated by activation of parabrachial neurons that contain CCK and ventromedial hypothalamic neurons that exhibit receptors to anorexic neuropeptide CCK and/or the hormone leptin. This grant proposal offers a unique collaborative effort of expertise from the field of feeding behavior and the field of pain and migraine. This interdisciplinary approach provides an opportunity to use state-of-the-art techniques to examine neuroanatomical, neurophysiological, molecular, and behavioral aspects of the neural mechanism that enables pain to induce anorexia; a biological phenomenon of distinct clinical relevance that affects millions of pain patients in the US.

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## • Project Title: NEUROPHYSIOLOGY OF CRANIAL HEADACHE

Principal Investigator & Institution: Strassman, Andrew M.; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

Timing: Fiscal Year 2001; Project Start 01-MAY-1996; Project End 31-MAR-2004

Summary: Description (adapted from applicant's abstract) **Headaches** that accompany intracranial pathologies as well as the **headache** of migraine are thought to result from mechanically or chemically induced activation or sensitization of sensory nerve fibers in the intracranial meninges. However, further understanding of the mechanisms of **headaches** is limited by the lack of information regarding the response properties of meningeal sensory fibers. The long-term goal of this research is to identify the types of stimuli and physiological conditions that excite meningeal primary afferent neurons and to investigate the pharmacological mechanisms by which their excitation may be suppressed. Five Specific Aims are proposed to examine the response of both pial and dural afferents. Specific Aim 1 will characterize the physiological response properties of

sensory afferents supplying the middle cerebral artery using graded mechanical and chemical stimuli. Specific Aim 2 will determine the effects of increased intracranial pressure and inflammation on the response properties of meningeal afferents that innervate the dural venous sinuses and middle cerebral artery. Specific Aim 3 will determine the effects of 5HT1B/D agonists on mechanical- and chemical-induced sensitized meningeal afferents. Specific Aim 4 will determine the effects of selective calcium channel blockers on mechanical- and chemical-induced sensitized meningeal afferents. Specific Aim 5 will determine the effects of acute spreading depression on mechanical- and chemical-induced sensitized meningeal afferents.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

#### Project Title: NITRIC OXIDE AND CHRONIC RHINOSINUSITIS

Principal Investigator & Institution: Jacob, Abraham; Otolaryngology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

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

Summary: (provided by applicant): Rhinosinusitis affects about 10% of the U.S. population and is the reason for approximately 12-million physician office visits annually. Obstruction to sinus drainage and immune dysregulation are believed to result in mucosal disruption and hypersecretion, nasal obstruction, postnasal discharge, cough, headache, and facial pressure. Our laboratory has successfully developed and described the first mouse model of chronic rhinosinusitis. Now in press, we plan to use this model to characterize this disease at its molecular and genetic levels. Since the discovery of its role in regulating vascular tone, nitric oxide (NO) and nitric oxide synthase (NOS) have been implicated in neurotransmission, ischemia-reperfusion syndromes, atopic diseases, and chronic inflammatory disorders. During health, it is known that the human paranasal sinuses are the dominant source of nitric oxide in the upper airways. However, the diseased state is not well characterized. While chemiluminescense measurements of NO in exhaled air indicate decreased levels during sinusitis, nasal secretions find increased NO metabolite concentrations. Although the literature implicates nitric oxide as a player, there is no consensus as to its precise role or its degree of importance. Further study is necessary. The in vivo analysis of nitric oxide's role in chronic sinonasal disease shall be investigated using 3 experimental groups of mice: C57BL/6 wild-type mice, NOS I, II, and III knockout mice, and C57BL/6 mice infused with aminoguanidine - a pan-NOS inhibitor. Each of these groups shall be further sub-divided into normal controls, sham-operated controls, and animals with surgically induced sinusitis. All groups and interventions shall be compared at the light microscope level. Histomorphometric analysis of en-bloc sinonasal tissue shall be used to quantify epithelial thickness, cell density, basement membrane thickness, and goblet cell number. Qualitative observations shall assess the presence or absence of inflammatory infiltrates and sinonasal fibrosis. With this approach of inhibiting nitric oxide production at multiple levels -- pharmacologically and with gene knockout -- we hope to better characterize the importance of NO in sinonasal pathophysiology.

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#### Project Title: NOVEL THERAPY FOR FEMALE SEXUAL DYSFUNCTION

Principal Investigator & Institution: Southan, Garry J.; Inotek Pharmaceuticals Corporation 100 Cummings Ctr, Ste 419E Beverly, Ma 01915

Timing: Fiscal Year 2001; Project Start 14-SEP-2001; Project End 30-SEP-2002

Summary: (provided by applicant): Female sexual dysfunction is increasingly recognized as a significant and widespread abnormality, contributing to coital pain, decreased libido, and a loss of sexual pleasure. In contrast to the enormous scientific investment in discovering methods to correct male sexual dysfunction, there has been virtually no attention directed at elucidating the fundamental mechanisms accounting for clitoral engorgement, vaginal lubrication, and alterations in vaginal and vulval mucosal blood flows accompanying sexual arousal. Increasing anatomic evidence points to a role for nitric oxide as a mediator of female genital hyperemia, similar to the situation in the male. Topical application of traditional nitric oxide donors to the female genitalia, however, produces profound systemic side effects, including headache and hypotension. What is needed is a potent, but regionally restricted nitric oxide donor, that acts on the local vaginal circulation exclusively. Towards this end, we have developed a nitric oxide pro-drug (DS1) that is restricted from transepithelial flux by virtue of its large hydrodynamic radius. Nitric oxide is released from DS1 and is able to traverse mucosal surfaces and vasodilate underlying arteriolar beds, whereas the prodrug cannot traverse the epithelium and is confined to the apical mucosa. Nitric oxide that reaches the systemic circulation is immediately inactivated by hemoglobin and therefore does not circulate as a systemic vasodilator. Thus, DS1 represents a true "regional" vasodilator. We have obtained preliminary data in rats that topical DS1 applied to the vaginal mucosa produces profound and immediate increases in vaginal blood flow, with no effect on systemic blood pressure. Utilizing an anesthetized rat model, we now propose to obtain a pharmacodynamic profile of DS1. We will simultaneously compare the regional blood flow and the mean peripheral arterial pressure in order to verify regional selectivity. Justification of further development towards commercialization will require 1) no decrease in systemic blood pressure, 2) >100 percent increase in vaginal blood flow, and 3) duration of regional hyperemia >30 minutes. PROPOSED COMMERCIAL APPLICATION: NOT AVAILABLE

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### Project Title: OPIATE MODULATION OF CORNEA PAIN PATHWAYS

Principal Investigator & Institution: Bereiter, David A.; Research Professor; Rhode Island Hospital (Providence, Ri) Providence, Ri 02903

Timing: Fiscal Year 2001; Project Start 01-APR-1988; Project End 31-JUL-2004

Summary: (Adapted from the Investigator's Abstract): The trigeminal nerve mediates pain sensation from craniofacial tissues including specialized structures such as the teeth, dura, and cornea. Pain that occurs during toothache, headache, and dry eye syndrome is a prevalent health problem, arises from varied etiology and often is difficult to manage. In addition to sensation, other aspects of pain (autonomic/endocrine reflexes, endogenous pain controls) can be altered by persistent trigeminal pain conditions. This proposal uses neurophysiological methods to test the central hypothesis that distinct groups of brainstem neurons mediate different aspects of corneal pain and that these neurons can be identified by their encoding properties, response to analgesic drugs, and efferent projection status. Specific Aim 1 defines the properties of trigeminal brainstem neurons that encode different corneal stimulus modalities (chemical, mechanical, cold). Corneal units that project to the sensory thalamus or superior salivatory nucleus/facial nucleus region are presumed to serve a role in sensory-discriminative or reflex autonomic/somatomotor functions, respectively. Specific Aims 2 and 3 assess the role of the longitudinal fiber system that connects rostral and caudal portions of trigeminal subnucleus caudalis in different aspects of cornea pain processing. Specific Aim 4 tests the hypothesis that receptors for glutamate mediate corneal input to trigeminal subnucleus caudalis and are necessary for the modulation of evoked activity seen after morphine. Specific Aim 5 tests the hypothesis that mu opioid agonists such as morphine act at sites outside the trigeminal brainstem complex to enhance corneal units at rostral portions of subnucleus caudalis and inhibit corneal units at the most caudal portions of subnucleus caudalis. These results will provide new information on the properties of trigeminal neurons that mediate the sensory-discriminative and ocular-specific reflex aspects of corneal pain and will lead to a better understanding of the brainstem organization that underlies craniofacial pain processing.

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#### Project Title: PAIN IN ADOLESCENTS: BIOLOGIC/PSYCHOSOCIAL RISK FACTORS

Principal Investigator & Institution: Leresche, Linda A.; Research Professor; University of Washington Seattle, Wa 98195

Timing: Fiscal Year 2001; Project Start 01-JAN-1989; Project End 31-AUG-2004

Summary: We propose a five-year program of research aimed at assessing the prevalence and incidence of temporomandibular disorder (TMD) pain, headache, back pain, and abdominal pain in adolescents., and identifying risk factors for onset of each of these common pain {{symptoms}}. Because the prevalence of headache and TMD pain is much higher in adult women than in adult men, the studies are designed to test the global hypothesis that this prevalence differences begin in adolescence and are associated with the hormonal change of puberty. The specific aims of study 1 are: 1) In a telephone survey, assess the prevalence, severity and temporal characteristics of TMD pain, headache, backpain and abdominal pain in an age- and sex-stratified random sample of adolescents, ages 11-17 (final n= 2970) from a defined population; 2) Identify potential risk factors for pain at each of these four sites; 3) Conduct standardized examinations and interviews for all respondents reporting TMD pain, as well as a sample of those without TMD pain (expected n's = 130 per respondents reporting TMD pain, as well as a sample of those without TMD pain (expected n's = 130 peer group) in order to: a) compare the rates of clinical signs and symptoms of temporomandibular disorders in cases and controls, and b) estimate the prevalence of specific clinical subtypes of TMD (myofascial pain, disc displacements, arthralgia, arthritis/arthrosis) using standardized examination methods and diagnostic algorithms. Examinations will be conducted in subjects' homes by Registered Dental Hygienists training and calibrated for reliability. The specific aims of Study 2 are: 1) Follow the cohort of 11 year old respondents from Study 1 (n= 1902) over a 3-year follow up period, using brief mail-in surveys and more extensive follow up data collection at 18 months and 3 years. Monitor rates of onset of TMD pain, headache, back pain and abdominal pain. Assess the impact of these pain problems in terms of interference with activities, use of medications and rates of health care use for pain; 2) Identify risk factors for onset of {{TMD pain, headache, back and abdominal pain}> Hypothesized risk factors for all pains include: female gender, number of existing pain complaints, and other somatic symptoms, numbers of health care visits in the prior year, and psychological distress; in addition, we hypothesize that sexual maturity is a risk factor for onset of TMD pain and headache; 3) Estimate rates of offset and recurrence of each of the pain c90mpliants over the 3-year follow up period; and, 4) Conduct examinations of the incidence cases of TMD pain, using examination methods and diagnostic algorithms as described for Study 1, to estimate the prevalence of specific subtypes of TMD.

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# • Project Title: PATIENT OUTCOMES: QUALITY OF LIFE AND LOST PRODUCTIVITY

Principal Investigator & Institution: Lofland, Jennifer H.; Administration; Thomas Jefferson University Office of Research Administration Philadelphia, Pa 191075587

Timing: Fiscal Year 2001; Project Start 01-MAR-2001; Project End 28-FEB-2005

Summary: Jennifer H. Lofland, PharmD and David B. Nash, MD, MBA from Thomas Jefferson University's Office of Health Policy and Clinical Outcomes, and Donald M. Steinwachs, PhD from Johns Hopkins School of Hygiene and Public Health, Department of Health Policy and Management propose a collaborative study for the mentored clinical scientist development award. With didactic and experimental components, this four-year career development plan will provide Jennifer H. Lofland with the skills necessary to meet her long-term objectives to be an independent health services researcher. The didactic component will be completed at Johns Hopkins University. The experiential component will measure and evaluate patient-focused outcomes: healthrelated quality of life and lost workplace and non-workplace productivity. The research objectives are to 1) validate a patient-focused headache questionnaire, 2) determine patient outcomes using the validated questionnaire, 3) determine methodologies for valuing lost productivity, 4) develop predictive models to determine the variables associated with decreased health-related quality of life and increased lost productivity for patients with asthma or with **headache**, and 5) develop a proposal for a healthcare program to improve patients' health-related quality of life and decreased lost productivity. The study population will include patients from the Jefferson Healthcare System and a Medicaid managed care organization. Information from this investigation may be used by clinicians and healthcare decision-makers to develop programs that can increase patients' health-related quality of life and decrease patients' lost workplace and non-workplace productivity.

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# Project Title: PERIMENOPAUSAL SYMPTOMS MANAGEMENT WITH ACUPUNCTURE

Principal Investigator & Institution: Cohen, Susan M.; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

Timing: Fiscal Year 2001

Summary: We propose to test the use of acupuncture for menopausal symptom relief for women who experience menopause following treatment for breast cancer. The study is designed to test the effect of acupuncture on the menopausal symptom of hot flashes, explore the anticipated treatment benefit of acupuncture on menopausal symptoms of mood changes, sleep disturbances, loss of concentration, joint pain, **headache** and nervousness as well as changes in ovarian hormones and quality of life, and increase the knowledge base concerning the effectiveness of alternative/complementary health practices.

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# • Project Title: PERMANENT MAGNETS IN THE TREATMENT OF CHRONIC TENSION HEADACHE

Principal Investigator & Institution: Henry, Katherine; New York University School of Medicine 550 1St Ave New York, Ny 10016

Timing: Fiscal Year 2001

Summary: This abstract is not available.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

#### Project Title: PHOTOPHYSICAL PROPERTIES OF TRICYCLIC ANTIEPILEPTIC DRUGS

Principal Investigator & Institution: Garcia, Carmelo; University of Puerto Rico at Humacao Box 428, Barrio Tejas Humacao, Pr 00791

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

Summary: The intense research devoted over the last few years to the study of epilepsy and antiepileptic drugs (AEDs) has only dealt with the physiology of the disease. This quality research has been aimed to replace the older AEDs with broad activity profiles and several severe side effects with new AEDs with better defined mechanism of action and fewer side effects. Nevertheless, most of these drugs still produce serious adverse reactions, including among others, dizziness, ataxia, somnolence, headache, blurred vision, nausea, vomiting, skin, allergy and photosensitization. The molecular photochemical mechanisms for the photosensitizing ability of some AEDs has never been studied, even through it was reported over ten years ago. Recent studies on the laser flash phototysis of related neuroleptic drugs (imipramine) showed that the triplet state can be efficiently quenched by the protons in the solution. The effectiveness of the quenching is very sensitive to the structure of the drug and seems to be involve in their phototoxicity. We propose to perfor the same set of experiments on several phototoxic antiepileptics. The goal of this project is to measure the photophysicat properties of a selected group of tricydic antiepileptic drugs and to study their short-lived transients. Special attention will be given to those transients associated with adverse effects in vivo: the cation radical, the first triplet excited state and singlet oxygen, Basic UV-Vis and luminescence techniques will be employed to study their absorption/emission properties. The transients will be characterized using optical absorption measurements with a Nd-YAG laser set-up. For the triplet state of these compounds, the extinction coefficient and the quantum yield will be determined using a comparative method and the triplet-triplet energy transfer principle, respectively. The triplet state will be bleached with a second delayed pulse to elucidate the reaction mechanism of these u'ansients. Combined MM+/PM3/RHF theoretical calculations will be performed with HyperCHEM (TM) 7.0 on the whole set of photophysical parameters, The theoretical values will be correlated with the experimental ones. The major goal of this project is to find a molecular/photophysical descriptor for the phototoxic side effect of tricydic antiepileptics.

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### Project Title: PULSE IV GLUCOCORTICOID INFUSION AS INITIAL TREATMENT OF GIANT CELL ARTERITIS

Principal Investigator & Institution: Mazlumzadeh, Mehrdad; Mayo Clinic Rochester 200 1St St Sw Rochester, Mn 55905

#### Timing: Fiscal Year 2001

Summary: Giant Cell Arteritis (GCA, temporal arteritis) is a vasculitis of the medium and large-sized arteries that usually presents with **headache** and visual disturbances in patients over the age of fifty. Conventional treatment with oral glucocorticoid (GC, steroid, prednisone) for up to two to three years has been the only known efficacious therapy to suppress the inflammatory process and prevent associated vascular complications. However, the long duration and the cumulative dose of GC therapy frequently results in multiple adverse effect. Recent studies have shown several relapses and persistence of inflammation based on elevated inflammatory markers such as interleulin-6 despite timely oral GC therapy. Investigations on animal models suggest the need for much higher doses of GC to appropriately treat the vasculitic process. This forms the basis of our proposed study which is a randomized, double-blinded, placebocontrolled, prospective clinical trial where biopsy proven GCA patients will be treated with high dose pulse intravenous (IV) GC initially followed by lower doses of oral GC. We hypothesize that this will result in shorter length of therapy with lower dose of GC and hence reduced adverse effects.

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### Project Title: QUANTITATIVE MRI AND 1H-MRS IN TRAUMATIC BRAIN INJURY

Principal Investigator & Institution: Grossman, Robert I.; Louis Marx Professor and Chairman; Radiology; New York University School of Medicine 550 1St Ave New York, Ny 10016

Timing: Fiscal Year 2001; Project Start 15-SEP-2000; Project End 31-JUL-2005

Summary: (Adapted from Applicant's Abstract): Traumatic brain injury 9TBI) has an incidence of nearly 2,000,000 cases per year, and is the leading cause of disability and death in children and young adults (peak incidence in 15 to 24 year olds) in the United States. Following mild head injury patients may suffer from a multitude of cognitive deficits including decreased speed in information processing, poor attention, concentration, and memory, and impaired logical reasoning skill, as well as more focal deficits including impairment of language or constructional abilities. A variety of other symptoms including headache, dizziness, nausea, neurasthenia, hyperesthesia, and emotional liability are commonly perceived. Head injury has been associated with shortterm increased b-amyloid protein deposition and long-term neurotic plaques characteristic of Alzheimer's Disease. Epidemiological studies have observed a statistically-significant relationship between TBI and the subsequent onset of AD. Indeed, there is growing evidence that head injury, even mild in nature, may have greater consequences than previously assumed. The investigators hypothesize that mild/moderate TBI can cause neuronal cell death (reflected primarily by gray matter volume lose) and that this is the primary factor in induction and progression of neurocognitive disability in head injured patients. The central hypothesis is to test this hypothesis that the investigators have developed and validated computerized quantitative methods based upon magnetic resonance (MR) imaging (MRI) to measure the effect of TBI on brain substance. The investigators have also devised and implemented a proton (+H) magnetic resonance spectroscopy (MRS) technique to quantitative the neuronal concentration of the entire brain based upon the measurement of N-acetylaspartate (WBNAA) which is considered to be a marker of neuronal integrity. This proposal will correlate these quantitative MR measures with clinical measures of disability and neurocognitive tests. The overarching goal is to utilize MRI and 'H MRS to detect and quantify the effects TBI in a well-characterized cohort of mild/moderate head injured patients over a duration of 5 years. The results from this research will provide new and important information regarding the full extent of TBI, aid in categorizing these patients, and serve as an arbiter to assess proposed treatment strategies.

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# • Project Title: RACE IN PHYSICIAN DECISION TO PRESCRIBE OPIOID ANALGESIA

Principal Investigator & Institution: Sarver, Joshua H.; Metrohealth System 2500 Metrohealth Dr Cleveland, Oh 44109

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

Summary: (provided by applicant) Several studies have shown that racial and ethnic minorities are less likely to receive analgesics. This study presents a theoretical framework for understanding these differences. The aim of this study is to begin to test this framework by conducting a series of mail surveys with case scenarios to determine: 1) the effect of race on physicians? use of analgesics for 3 acute, painful conditions (back pain with sciatica, ankle fracture, and migraine headache); 2) whether providing information on patients? socioeconomic status, role impairment, and likelihood that narcotics might be misused mitigates the effect of race on physicians? decisions to prescribe analgesics; and 3) whether physician characteristics are related to differential treatment of racial and ethnic minorities. Phase 1 of this study will determine clinical factors that influence physicians? decisions to prescribe opioid analgesics for the 3 conditions (regardless of patients? race/ethnicity) using individual physician interviews and a mail survey of 650 emergency department physicians. In phase 2, information from phase 1 will be used to construct scenarios that include information on the most important clinical factors affecting prescribing opioid analgesics. Two versions of each of the 3 scenarios will be constructed: 1) clinical factors plus race (race only); and 2) clinical factors, race, and information on patients? socioeconomic status, role impairment, and likelihood that narcotics might be misused (race plus). These scenarios will be mailed in random order to 6075 emergency department physicians. Responses will be analyzed to determine whether racial and ethnic minorities are less likely to receive opioids with the race only scenarios (Aim 1), whether any difference in treatment persists for the race plus scenarios (Aim 2), and whether physician characteristics obtained from the phase 2 mailing explain lower use of opioid analgesics (Aim 3). This study moves investigation beyond documentation of racial disparities in treatment and toward theory based hypothesis testing. Understanding the causes of racial disparities will permit careful development of targeted interventions to address possible racial disparities in physician treatment decisions.

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#### • Project Title: RACE, PSYCHIATRIC DISORDERS, AND HEADACHE

Principal Investigator & Institution: Heckman, Bernadette D.; Psychology; Ohio University Athens Athens, Oh 45701

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

Summary: (provided by applicant): This application requests five years of support for a Mentored Research Scientist Development Award (K01) for a new minority investigator. The objectives of the planned training program are two-fold. The first objective is to provide the minority candidate with contemporary training in the areas of statistics, research methodology, research ethics, the pathophysiology of **headache** disorders, cross-cultural psychology, and health disparities. Formal coursework in these areas will facilitate the successful conduct of the planned study and prepare the candidate for future research endeavors throughout her career. The second objective is to examine how race and psychiatric co-morbid conditions are related to **headache** severity, quality of life, treatment adherence, and ability to respond favorably to treatments in people with episodic migraines, chronic migraines, episodic tension-type **headaches**, chronic

tension-type **headaches**, substance abuse **headaches**, or cluster **headaches**. Using a quasi-experimental prospective research design, 400 patients presenting at outpatient medical centers in four urban areas of Ohio (Cincinnati, Cleveland, Columbus, and Toledo) will complete self-administered assessments, telephone-based interviews, and daily **headache** diaries that elicit data on **headache** severity, quality of life, social support, treatment self-efficacy, locus of control, treatment adherence, and treatment outcome. Guided by Social Cognitive Theory (SCT; Bandura, 1986), the planned study will employ structural equation modeling path analysis to determine whether SCT constructs, such as social support, health-related locus of control, and treatment self-efficacy, mediate associations between race and the presence of a co-morbid psychiatric disorder and key outcome measures, such as quality of life and treatment outcome. If successful, the candidate will obtain extramural funding prior to the completion of the training program that will enable her to conceptualize, implement, and evaluate a culturally-contextualized intervention to reduce **headache** pain and improve the life quality of people who experience severe **headache** characteristics.

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# Project Title: RECOMBINANT HERPES INJECTION INTO TRIGEMINAL GANGLIA

Principal Investigator & Institution: Yeomans, David C.; Assistant Professor; Anesthesia; Stanford University Stanford, Ca 94305

Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-JUL-2005

Summary: (provided by applicant): Head cancer pain, trigeminal neuralgia, migraine headache, dental pain and temporomandibular joint pain are all examples of pain syndromes that are unique to the trigeminal system. In many instances, these pain types are hard to treat clinically, with last-line opiates working only marginally well in some instances, and not at all in others. In addition, the tolerance and addiction potential of strong, systemic opioids sometimes limit the duration over which they can be used effectively. Thus, there is a need for novel approaches to the treatment of trigeminal pain. We have previously demonstrated the potential of using replication-defective herpes viral constructs to alter the function of pain-sensing nerve cells, such that we have been able to produce robust, highly localized analgesia for months after a single application. In doing this we have applied the virus locally to targeted tissues, such as skin. Doing so, we have observed a very long-lasting (> 20 weeks) attenuation of pain responses limited to those areas treated with the virus. In many trigeminal syndromes however, pain is relatively diffuse or multicentered. Applications of vectors to peripheral tissues may be of limited utility in these cases, as a more widely distributed analgesic effect is desirable. One method that has not yet been investigated would be to inject vectors directly into the trigeminal ganglia, the grouping of neurons that make up the cell bodies of the sensory nerves of the trigeminal. In doing this, we would expect to introduce recombinant vectors over a wide distribution of trigeminal neurons, and thus, potentially, producing a widespread analgesic effect. The experiments described here will provide evidence as to whether direct trigeminal injection of recombinant herpes vectors, encoding genes for analgesic peptides, will alter the sensitivity to nociceptive stimulation of tissue innervated by the trigeminal. In so doing, we hope to provide initial support for what may be a new long-lasting treatment for trigeminal nerverelated pain.

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#### • Project Title: RENAL DENERVATION IN ORTHOSTATIC INTOLERANCE

Principal Investigator & Institution: Biaggioni, Italo; Professor of Medicine and Pharmacology; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

Timing: Fiscal Year 2001

Summary: Orthostatic Intolerance is a syndrome more common in women than men and typically seen in younger rather than older patients. It is typified by postural tachycardia. Orthostatic symptoms include lightheadedness, fatigue, nausea, tremulousness, and alterations in vision such as tunnel vision or blurring. Less commonly patients complain of anxiety, **headache**, acral pain or coolness, and chest wall pain. Patients sometimes have postural hypotension although this isn't as marked as the postural tachycardia would suggest. Up to fifty percent of patients have had an antecedent viral illness prior to developing orthostatic intolerance. This will assess renal hemodynamics and other indicators of sympathetic activity in response to head up tilit and Trimethaphan infusion in orthostatic patients with low plasma renin activity, patients with high plasma renin activity and normals, and assess response to a low sodium diet in orthostatic intolerance patients with low plasma renin activity, patients with high plasma renin activity and normals.

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### • Project Title: SEROTONIN 1B AND 1D RECEPTORS IN HEAD PAIN

Principal Investigator & Institution: Potrebic, Sonja B.; Neurology; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

Timing: Fiscal Year 2001; Project Start 01-JAN-2001; Project End 31-DEC-2003

Summary: (Applicant's Abstract): The pathophysiology of migraine, a common disorder causing significant disability and economic burden, is still poorly understood. The development of selective agonists for serotonin (5HT) 1B and 5HT1D receptors (5HT1B/1D agonists) has revolutionized headache treatment. The effectiveness of these medications suggests that understanding their mechanism of action will advance knowledge about the etiology of migraine headache. The general aim of this proposal is to elucidate neural mechanisms that mediate the therapeutic effects of selective 5HT1B/1D agonists. To achieve this goal, a series of anatomical and electrophysiological animal studies are proposed. The experiments will determine the distribution and neurotransmitter co-localization of sensory ganglion cells possessing 5HT1B and 5HT1D receptors through use of immunohistochemistry. The distribution and origin of these receptors to intracranial and extracranial structures will be compared by combining retrograde tracing with immunohistochemistry. Experiments utilizing in vivo extracellular electrophysiological techniques will explore functional correlates of anatomic innervation. The experiments will focus on determining whether intracranial vascular structures posses an innervation that is unique in terms of 5HT1B and/or 5HT1D receptors. A clinical study will test the proposed selectivity of 5HT1B/1D agonists for migraine and cluster headache.

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#### Project Title: STRUCTURAL ELUCIDATION OF THE 5HTLA RECEPTOR-G PROTEIN INTERFACE

Principal Investigator & Institution: Parker, Keith K.; University of Montana University Hall 202 Missoula, Mt 598124104

Timing: Fiscal Year 2001

Summary: Structural Elucidation of the 5HT1a Receptor-G Protein Interface The serotonin1a (5HT1a) receptor is centrally involved in various human disorders including depression, anxiety, obsessive-compulsive disorder, and migraine headache. The receptor is a member of the superfamily of seven transmembrane domain, G protein-coupled receptors. By agonist stimulation of receptor, G protein is activated, which in turn regulates cellular effectors such as adenyl cyclase. Through these events, informational signal is transduced into cellular changes which underlie drug effect at the biochemical level. In this project, the focus is on events surrounding the key interaction between receptor and G protein. A peptide from the transmembrane 5/intracellular loop 3 region of the human 5HT1a receptor, and substitution and truncation derivatives of this peptide are used as probes of the receptor/G protein interface. The peptide's abilities to activate inherent properties of the G protein, such as incorporation of GTP into the G protein, and GTPase activity, are quantified. By crosslinking, regions of the G protein responsible for coupling to the receptor will be identified. Finally, selected peptides which have demonstrated outstanding activity in these tests will be used for high resolution spectral studies. Circular dichroism of the peptides will be measured in solution to determine conformations of the peptide as it approaches G protein prion to coupling. Once coupled, multi- dimensional NMR of the peptide/G protein complex will determine conformations which lead to G protein activation. Information gathered in these experiments will form the basis for development of models of 5HT1a receptor peptide/G protein interaction. In the long range, structural lessons learned from the human 5HT1a receptor/G protein system will add to growing knowledge of receptor/G protein events in the receptor superfamily. Better structural and biochemical understanding of these receptors will help in elucidating receptor pathology in detail, which in turn should assist in better understanding of important human disease processes. Additionally, development of understanding of at receptor/G protein interactions will potentially lead to therapeutic approaches targeted at pathologies in the sequence of signal transducing events.

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#### Project Title: SYNAPTIC DEFECTS IN THE CA CHANNEL MUTANT MOUSE

Principal Investigator & Institution: Dunlap, Kathleen; Professor; Physiology; Tufts University Boston Boston, Ma 02111

Timing: Fiscal Year 2001; Project Start 01-JUN-2001; Project End 31-MAY-2005

Summary: adapted from applicant's abstract) Naturally-occurring mutations in the gene encoding class A (or P/Q-type) calcium channels are associated with multiple abnormalities, ranging from migraine headache to motor ataxias to absence epileptic seizures. These heterogeneous neurological phenotypes underscore the central importance of P/Q-type calcium channels-the dominant exocytotic channels in central nervous system. P/Q is not, however, the only type of calcium channel controlling synaptic transmission in the CNS. N-type (or class B) calcium channels usually co-exist with P/Q and, together, they jointly govern the release of many, if not all, transmitters. Whether P/Q and N channels play unique functional roles at the synapse is unclear. Experiments with one P/Q channel mutant mouse, tottering, suggest, however, that the two channels are not functionally redundant and that tottering offers an opportunity to explore their different roles in exocytosis. Homozygous tottering animals display a dramatic neurological phenotype, characterized by ataxia and frequent absence seizures. Our preliminary experiments on tottering demonstrate that a primary consequence of the P/Q channel mutation is a shift in the ratio of P/Q:N channels in some (but not all) nerve terminals. For example, release of the excitatory transmitter glutamate and glutamatergic synaptic transmission at the parallel fiber-Purkinje cell synapse in cerebellum are controlled largely by N-type calcium channels in the mutant, rather than P/Q-type as they are in wild-type animals. As a consequence of these changes in the presynaptic calcium channel complement, excitatory transmission is reduced and G protein-dependent inhibition is enhanced at mutant synapses. In contrast, GABA release from inhibitory nerve terminals appears to be unaffected in tottering animals. On the basis of these observations, we hypothesize that the selective effect of the tottering allele on excitatory transmission leads to an overall decreased excitation of Purkinje cells. Three interacting factors contribute: 1) glutamate release from excitatory inputs is impaired due to the decreased involvement of P/Q channels; 2) the relative increase in N channel-mediated release further enhances susceptibility of these inputs to presynaptic inhibition (because N channels are more effectively modulated by G proteins than are P/Q channels); and 3) unimpaired inhibitory, GABAergic inputs are relatively more efficacious in the face of reduced excitation. As Purkinje cells control cerebellar output via GABAergic inhibitory transmission onto output neurons in deep cerebellar nuclei, we predict that a reduction in Purkinje cell activity will enhance net cerebellar output. Ultimately, such changes would excite thalamus and motor cortex, providing a plausible mechanism for the ataxia and seizures observed in these animals. Experiments proposed here will stringently test this hypothesis through in-depth cellular and synaptic exploration of calcium channels and calcium-dependent exocytosis in tottering cerebellum. Results will provide essential information for understanding the consequences of the mutation on cerebellar circuit behavior and may, in the long term, offer suggestions for new therapeutic interventions into ataxia and other motor disorders.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

# • Project Title: TAILORED MESSAGING AND SELF DIRECTED HEADACHE TREATMENT

Principal Investigator & Institution: Nicholson, Robert A.; Miriam Hospital Providence, Ri 02906

Timing: Fiscal Year 2001; Project Start 17-SEP-2001

Summary: Migraine **headache** is a prevalent health problem that negatively impacts the sufferer's ability to function at work and with family and friends. Self-directed treatments are a way to reach a large number of migraine sufferers, many of whom do not seek services and remain in need of treatment. However, these interventions often suffer from attrition and an inability to address specific needs of the headache sufferer. Incorporating tailored messaging into self-directed behavioral treatment may provide a way to overcome the obstacles that exist in the effective delivery of self-directed treatment protocols for headache. Tailored messaging, already used effectively in areas of health promotion, uses informational and behavioral strategies designed to modify behaviors that influence one's health-related activities, and targets the specific needs of sufferers. The proposed study looks to develop and incorporate a tailored messaging system into a self- directed treatment for migraine headache. The specific aims of this proposal are to develop the tailored messages and the message algorithm to be used in the intervention, evaluate the impact of the intervention on headache activity and headache-related disability, determine whether headache-related beliefs mediate treatment effects, and evaluate the extent to which the tailored messages are perceived to be effective by the treatment recipients.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

### Project Title: TRIGEMINAL PAIN PATHWAYS

Principal Investigator & Institution: Aicher, Sue A.; Associate Scientist; None; Oregon Health & Science University Portland, or 972393098

Timing: Fiscal Year 2001; Project Start 01-FEB-1999; Project End 31-JAN-2003

Summary: Trigeminal afferents containing glutamate and/or substance P (SP) convey noxious input from orofacial regions to the dorsal horn of trigeminal nucleus caudalis (Vc). The postsynaptic effects of glutamate released from these terminals are partially mediated through the NMDA receptor and can be inhibited by ligands of the mu opiate receptor (muOR). Three specific aims of this proposal will examine the cellular substrates for potential function of the NMDA and muORs in the rat trigeminal dorsal horn using electron microscopic immunocytochemistry. Aim 1a will test the hypothesis that NMDA receptors are located within neurons postsynaptic to SP terminals, supporting the notion that agonists of the NMDA receptor facilitate the postsynaptic effects of SP on second-order neurons. Aim 1b will determine if muORs are contained within SP terminals, which would imply that the antinociceptive effects of muOR ligands can be attributed to direct modulation of SP release rather than to actions on interneurons. Aim 2 will examine the localization of NMDA receptors and muORs relative to trigeminothalamic and trigeminoparabrachial neurons that are known to be critical for the perception of **head pain**. These studies will use retrograde tracing from selected regions combined with immunocytochemical receptor localization. These experiments will test the hypotheses that: (a) NMDA receptors located on the plasma membranes of trigeminothalamic neurons are a substrate for glutamatergic excitation of these neurons; and (b) muORs on these cells are a potential substrate for antinociception. Preferential localization of receptors on cells projecting to thalamus may suggest models for targeted modulation of nociceptive transmission. Aim 3 will compare the subcellular localization of these receptors (NMDA and muOR) in normal and morphine tolerant rats. The muOR is critical for both the analgesia and tolerance produced by morphine and antagonists of the NMDA receptor can block morphine tolerance. These studies will determine if there is a change in receptor density and/or subcellular redistribution (e.g. shift of receptor from membrane to intracellular sites) that may be a mechanism for morphine tolerance. The experiments outlined in this proposal will demonstrate the subcellular localization of NMDA receptors and muORs in trigeminal nociceptive pathways which may be used as targets for new therapeutic strategies to control trigeminal pain, including tooth pain and headache.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

## • Project Title: VIRTUAL REALITY AND DRIVING ASSESSMENT AFTER TBI

Principal Investigator & Institution: Schultheis, Maria T.; Kessler Medical Rehab Res & Educ Corp Research & Education Corp. West Orange, Nj 07052

Timing: Fiscal Year 2001; Project Start 01-APR-2001

Summary: Recently, researchers have begun to investigate the potential of virtual reality (VR) technology in various aspects of the medical field, including cognitive rehabilitation (CR). These studies suggest that, through its unique ability to present objective, ecologically valid stimuli in an interactive and easily-modifiable environment, VR offers tremendous new opportunities for CR. However, to date, only a handful of these studies integrating VR and CR have included clinical populations, and most have been limited to the assessment of component cognitive abilities (i.e. memory, visual-spatial abilities) and/or the evaluation of simple cognitive tasks. One area within CR, which can exemplify VR's potential in assessing complex cognitive behavior, but which

remains minimally investigated, is the assessment of driving ability in individuals with traumatic brain injury (TBI). In the current proposal, I plan to directly examine VR's potential in the assessment of driving ability by comparing a VR driving protocol to a current driving assessment protocol, the behind-the-wheel evaluation (BTW) at two levels: 1) comparison of overall performance and 2) comparison to performance of specific responses/behaviors recorded during the behind-the-wheel evaluation. In addition, by investigating the effects of VR exposure through the use of a standardized questionnaire (i.e., Simulator Sickness Questionnaire), the proposed study will address the need for further understanding of the impact of VR environments on clinical populations.

Website: http://crisp.cit.nih.gov/crisp/Crisp\_Query.Generate\_Screen

## E-Journals: PubMed Central<sup>3</sup>

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).<sup>4</sup> Access to this growing archive of e-journals is free and unrestricted.<sup>5</sup> To search, go to http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Pmc, and type "headache" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for headache in the PubMed Central database:

• Aspirin for prophylaxis against headache at high altitudes: randomised, double blind, placebo controlled trial. by Burtscher M, Likar R, Nachbauer W, Philadelphy M.; 1998 Apr 4;

http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=28508

- Class-action lawsuits medicine's newest legal headache. by Lightstone S.; 2001 Sep 4; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=81425
- Does bed rest after cervical or lumbar puncture prevent headache? A systematic review and meta-analysis. by Thoennissen J, Herkner H, Lang W, Domanovits H, Laggner AN, Mullner M.; 2001 Nov 13; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=81623
- Headaches due to arachnoid leak. by Parkinson D.; 2002 Apr 16; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=100863
- Ice cream evoked headaches (ICE-H) study: randomised trial of accelerated versus cautious ice cream eating regimen. by Kaczorowski M, Kaczorowski J.; 2002 Dec 21; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=139031
- **Prevalence of migraine headache in Canada.** by Martin S.; 2001 May 15; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=81088

<sup>&</sup>lt;sup>3</sup> Adapted from the National Library of Medicine: http://www.pubmedcentral.nih.gov/about/intro.html.

<sup>&</sup>lt;sup>4</sup> 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.

<sup>&</sup>lt;sup>5</sup> 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.

- Prevention of headache after lumbar puncture: questionnaire survey of neurologists and neurosurgeons in United Kingdom:. by Serpell MG, Haldane GJ, Jamieson DR, Carson D.; 1998 Jun 6; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=28569
- Relation between headache in childhood and physical and psychiatric symptoms in adulthood: national birth cohort study. by Fearon P, Hotopf M.; 2001 May 12; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=31590
- Rheumatoid arthritis viewed using a headache paradigm. by Holmdahl R.; 2000; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=129997
- Working with movie stars may cause legal headache, CMPA warns. by Sullivan P.; 2002 Sep 3;

http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=121992

## 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.<sup>6</sup> 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 headache, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "headache" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for headache (hyperlinks lead to article summaries):

- A 32-year-old Brazilian woman with severe headache and fever. Author(s): Goldani LZ.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 2002 December 15; 35(12): 1512, 1549-50. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12474856&dopt=Abstract
- A case of dizziness, headache, aural fullness, and concentration difficulty following scuba diving.

Author(s): Brookler KH. Source: Ear, Nose, & Throat Journal. 2003 May; 82(5): 356-8. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12789759&dopt=Abstract

<sup>&</sup>lt;sup>6</sup> 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 community-based study of headache diagnosis and prevalence in Singapore. Author(s): Ho KH, Ong BK. Source: Cephalalgia : an International Journal of Headache. 2003 February; 23(1): 6-13. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12534573&dopt=Abstract
- A comparison of familial and sporadic migraine in a headache clinic population. Author(s): Rainero I, Valfre W, Gentile S, Lo Giudice R, Ferrero M, Savi L, Pinessi L. Source: Funct Neurol. 2002 October-December; 17(4): 193-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12675262&dopt=Abstract
- A group of cranio-cervical acceleration/deceleration trauma patients who developed chronic post-traumatic headache.

Author(s): Fishbane DA.

Source: European Spine Journal : Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2002 December; 11(6): 606.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12530361&dopt=Abstract

- A headache diagnosis project. Author(s): Pryse-Phillips W, Aube M, Gawel M, Nelson R, Purdy A, Wilson K. Source: Headache. 2002 September; 42(8): 728-37. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12390635&dopt=Abstract
- A randomized controlled trial of exercise and manipulative therapy for cervicogenic headache.

Author(s): Jull G, Trott P, Potter H, Zito G, Niere K, Shirley D, Emberson J, Marschner I, Richardson C.

Source: Spine. 2002 September 1; 27(17): 1835-43; Discussion 1843. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12221344&dopt=Abstract

• A response to 'Post dural puncture headache', Davies J R, Anaesthesia 2003; 58: 398. Author(s): Butler P.

Source: Anaesthesia. 2003 August; 58(8): 829. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12859518&dopt=Abstract

 Abnormal neuromuscular transmission in cluster headache. Author(s): Ertas M, Baslo MB. Source: Headache. 2003 June; 43(6): 616-20. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12786920&dopt=Abstract • Academic headache medicine in America: report of academic membership survey of the American Headache Society special interest section on academic affairs. Author(s): Finkel AG.

Source: Headache. 2003 March; 43(3): 266-71.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12603646&dopt=Abstract

 Acute and chronic hypertensive headache and hypertensive encephalopathy. Author(s): Gronbaek E.
Source: Cephalalgia : an International Journal of Headache. 2003 April; 23(3): 238-9; Author Reply 239. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12662195&dopt=Abstract

• Acute headache as a presenting symptom of tacrolimus encephalopathy. Author(s): Kiemeneij IM, de Leeuw FE, Ramos LM, van Gijn J. Source: Journal of Neurology, Neurosurgery, and Psychiatry. 2003 August; 74(8): 1126-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12876250&dopt=Abstract

• American Headache Society members' assessment of headache diagnostic criteria. Author(s): Nash JM, Lipchik GL, Holroyd KA, McCool H, Stensland M; American Headache Society.

Source: Headache. 2003 January; 43(1): 2-13. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12864752&dopt=Abstract

• Amlodipine reduces blood pressure and headache frequency in cocaine-dependent outpatients.

Author(s): Malcolm R, Liao J, Michel M, Cochran K, Pye W, Yeager D, Halushka PV. Source: J Psychoactive Drugs. 2002 October-December; 34(4): 415-9. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12562110&dopt=Abstract

### • An Unusual Headache: Lemierre's Syndrome.

Author(s): Tan NC, Tan DY, Tan LC. Source: Journal of Neurology. 2003 February; 250(2): 245-6. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12622096&dopt=Abstract

• Analysis of nitric oxide synthase genes in cluster headache. Author(s): Sjostrand C, Modin H, Masterman T, Ekbom K, Waldenlind E, Hillert J. Source: Cephalalgia : an International Journal of Headache. 2002 November; 22(9): 758-64.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12421162&dopt=Abstract

• Analysis of the patients attending a specialist UK headache clinic over a 3-year period.

Author(s): Dowson AJ. Source: Headache. 2003 January; 43(1): 14-8. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12864753&dopt=Abstract

• Antidepressants in the treatment of migraine headache.

Author(s): Punay NC, Couch JR. Source: Current Pain and Headache Reports. 2003 February; 7(1): 51-4. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12525271&dopt=Abstract

 Antiepileptic drugs in the treatment of chronic headaches. Author(s): Agostoni E, Frigerio R, Santoro P. Source: Neurological Sciences : Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology. 2003 May; 24 Suppl 2: S128-31. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12811611&dopt=Abstract

• Application of the 1988 International Headache Society diagnostic criteria in nine Italian headache centers using a computerized structured record.

Author(s): Gallai V, Sarchielli P, Alberti A, Pedini M, Gallai B, Rossi C, Cittadini E; Collaborative group for the application of IHS criteria of the Italian society for the study of headache.

Source: Headache. 2002 November-December; 42(10): 1016-24.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12453033&dopt=Abstract

- Articular and muscular impairments in cervicogenic headache: a case report. Author(s): Petersen SM.
  Source: The Journal of Orthopaedic and Sports Physical Therapy. 2003 January; 33(1): 21-30; Discussion 30-2. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12570283&dopt=Abstract
- Aspirin in episodic tension-type headache: placebo-controlled dose-ranging comparison with paracetamol.

Author(s): Steiner TJ, Lange R, Voelker M. Source: Cephalalgia : an International Journal of Headache. 2003 February; 23(1): 59-66. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12534583&dopt=Abstract

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- Atypical presentations of cluster headache. Author(s): Rozen TD.
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- Backache, headache, and neurologic deficit after regional anesthesia. Author(s): Munnur U, Suresh MS. Source: Anesthesiology Clinics of North America. 2003 March; 21(1): 71-86. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12698833&dopt=Abstract
- Behavioral and psychologic aspects of the pathophysiology and management of tension-type headache.

Author(s): Holroyd KA. Source: Current Pain and Headache Reports. 2002 October; 6(5): 401-7. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12207853&dopt=Abstract

• Behavioral management of recurrent headache: three decades of experience and empiricism.

Author(s): Penzien DB, Rains JC, Andrasik F.

Source: Applied Psychophysiology and Biofeedback. 2002 June; 27(2): 163-81. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12206049&dopt=Abstract

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Author(s): Andrasik F.

Source: Neurological Sciences : Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology. 2003 May; 24 Suppl 2: S80-5. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12811599&dopt=Abstract

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Author(s): Boes CJ, Matharu MS, Goadsby PJ. Source: Cephalalgia : an International Journal of Headache. 2002 December; 22(10): 772-9. Review.

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Author(s): Cattin T. Source: N Z Med J. 2003 May 16; 116(1174): U440. No Abstract Available. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12766786&dopt=Abstract

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Author(s): Schulman EA. Source: Headache. 2002 November-December; 42(10): 1048-50. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12453039&dopt=Abstract

 Brief neurologist-administered behavioral treatment of pediatric episodic tensiontype headache.
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Source: Neurology. 2003 April 8; 60(7): 1215-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12682344&dopt=Abstract • Carnitine palmityltransferase II (CPT2) deficiency and migraine headache: two case reports.

Author(s): Kabbouche MA, Powers SW, Vockell AL, LeCates SL, Hershey AD. Source: Headache. 2003 May; 43(5): 490-5. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12752755&dopt=Abstract

 Case 1: a woman with headache and dizziness. Author(s): Gibbons C, Llinas R. Source: Medgenmed [electronic Resource] : Medscape General Medicine. 2003 February 13; 5(1): 35. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_

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• Case 33-2002: a 28-year-old woman with ocular inflammation, fever, and headache. Author(s): Siegel DM.

Source: The New England Journal of Medicine. 2003 January 30; 348(5): 474-6; Author Reply 474-6.

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http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12556554&dopt=Abstract

• Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 17-2003. A 38-year-old woman with fever, headache, and confusion. Author(s): Hirsch MS, Werner B. Source: The New England Journal of Medicine. 2003 May 29; 348(22): 2239-47. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12773652&dopt=Abstract

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- Cavernous sinus syndrome and headache due to bilateral carotid artery aneurysms. Author(s): Atri A, Sheen V.
  Source: Archives of Neurology. 2003 September; 60(9): 1327-8. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12975304&dopt=Abstract
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- Cerebrovascular reactivity in adolescents with migraine and tension-type headache during headache-free interval and attack. Author(s): Rosengarten B, Sperner J, Gorgen-Pauly U, Kaps M. Source: Headache. 2003 May; 43(5): 458-63. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12752750&dopt=Abstract
- Cervicogenic headache in children. Author(s): Ormos G. Source: Headache. 2003 June; 43(6): 693-4. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12786933&dopt=Abstract
- Chronic daily headache: identification of factors associated with induction and transformation.

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- Tizanidine is not a cure for chronic daily headache. Author(s): Warner JS. Source: Headache. 2003 March; 43(3): 296; Author Reply 296-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12603653&dopt=Abstract
- Topical agents in the treatment of cluster headache. Author(s): Markley HG. Source: Current Pain and Headache Reports. 2003 April; 7(2): 139-43. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12628056&dopt=Abstract
- Topiramate in the treatment of cluster headache. Author(s): McGeeney BE.
   Source: Current Pain and Headache Reports. 2003 April; 7(2): 135-8. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12628055&dopt=Abstract
- Transient minor improvement of high altitude headache by sumatriptan. Author(s): Utiger D, Eichenberger U, Bernasch D, Baumgartner RW, Bartsch P. Source: High Altitude Medicine & Biology. 2002 Winter; 3(4): 387-93. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12631424&dopt=Abstract
- Treating ECG changes during Caesarean section: is it worth the headache? Author(s): Ramachandran K, Srirangadarshan, Kapoor V. Source: Anaesthesia. 2003 March; 58(3): 293-4. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12603478&dopt=Abstract
- Treating headache in the emergency ward: avoiding the migraine-meperidine trap. Author(s): Gupta R, Gernsheimer J.
   Source: Annals of Emergency Medicine. 2003 July; 42(1): 161; Author Reply 161-2. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12852415&dopt=Abstract

.

## • Treatment of chronic daily headache with medication overuse.

Author(s): Grazzi L, Andrasik F, D'Amico D, Usai S, Rigamonti A, Leone M, Bussone G. Source: Neurological Sciences : Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology. 2003 May; 24 Suppl 2: S125-7. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12811610&dopt=Abstract

• Treatment of cluster headache with topiramate: effects and side-effects in five patients.

Author(s): Rapoport AM, Bigal ME, Tepper SJ, Sheftell FD. Source: Cephalalgia : an International Journal of Headache. 2003 February; 23(1): 69-70; Author Reply 70. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12534585&dopt=Abstract

## • Trigemino-cervical reflex in patients with headache.

Author(s): Milanov I, Bogdanova D. Source: Cephalalgia : an International Journal of Headache. 2003 February; 23(1): 35-8. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12534578&dopt=Abstract

**Trigeminofacial reflexes in primary headaches.** Author(s): Proietti Cecchini A, Sandrini G, Fokin IV, Moglia A, Nappi G. Source: Cephalalgia : an International Journal of Headache. 2003; 23 Suppl 1: 33-41.

Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12699457&dopt=Abstract

- Unexplained fitting in patients with post-dural puncture headache. Risk of iatrogenic pneumocephalus with air rationalizes use of loss of resistance to saline. Author(s): van den Berg AA, Nguyen L, von-Maszewski M, Hoefer H. Source: British Journal of Anaesthesia. 2003 June; 90(6): 810-1; Author Reply 811-2. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12765902&dopt=Abstract
- Unexplained fitting in three parturients suffering from postdural puncture headache. Author(s): Oliver CD, White SA. Source: British Journal of Anaesthesia. 2002 November; 89(5): 782-5. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12393783&dopt=Abstract
- Update on cluster headache. Author(s): May A, Leone M. Source: Current Opinion in Neurology. 2003 June; 16(3): 333-40. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12858070&dopt=Abstract

• Update on postdural puncture headache. Author(s): Davignon KR, Dennehy KC. Source: International Anesthesiology Clinics. 2002 Fall; 40(4): 89-102. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12409935&dopt=Abstract

• Upper and lower cluster headache: clinical and pathogenetic observations in 608 patients.

Author(s): Cademartiri C, Torelli P, Cologno D, Manzoni GC. Source: Headache. 2002 July-August; 42(7): 630-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12482215&dopt=Abstract

• Upper cervical anterior diskectomy and fusion improves discogenic cervical headaches.

Author(s): Schofferman J, Garges K, Goldthwaite N, Koestler M, Libby E. Source: Spine. 2002 October 15; 27(20): 2240-4. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12394901&dopt=Abstract

- Use of botulinum toxin type B for migraine and tension headaches. Author(s): Fadeyi MO, Adams QM.
   Source: American Journal of Health-System Pharmacy : Ajhp : Official Journal of the American Society of Health-System Pharmacists. 2002 October 1; 59(19): 1860-2. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12374073&dopt=Abstract
- Use of botulinum toxins for chronic headaches: a focused review. Author(s): Loder E, Biondi D.
   Source: The Clinical Journal of Pain. 2002 November-December; 18(6 Suppl): S169-76. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12569965&dopt=Abstract
- Use of willingness to pay to study values for pharmacotherapies for migraine headache.

Author(s): Lenert LA. Source: Medical Care. 2003 February; 41(2): 299-308. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12555057&dopt=Abstract

• Value of neuroimaging in the evaluation of neurologically normal children with recurrent headache.

Author(s): Alehan FK. Source: Journal of Child Neurology. 2002 November; 17(11): 807-9. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12585718&dopt=Abstract

- 84 Headache
- Variations among emergency departments in the treatment of benign headache. Author(s): Vinson DR, Hurtado TR, Vandenberg JT, Banwart L. Source: Annals of Emergency Medicine. 2003 January; 41(1): 90-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12514688&dopt=Abstract
- Volume and nature of telephone calls in a specialty headache practice. Author(s): Loder E, Geweke L. Source: Headache. 2002 October; 42(9): 883-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12390614&dopt=Abstract
- What works. Headache relief. Outsourcing credentialing for a busy physician practice brings improvement. Author(s): Brockette JT. Source: Health Management Technology. 2003 February; 24(2): 36-8.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12592727&dopt=Abstract

# **CHAPTER 2. NUTRITION AND HEADACHE**

## Overview

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

## **Finding Nutrition Studies on Headache**

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.<sup>7</sup> 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 "headache" (or synonyms) into the search box, and click "Go." To narrow the search, you can also select the "Title" field.

<sup>&</sup>lt;sup>7</sup> 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 "headache" (or a synonym):

- A negative trial of sodium valproate in cluster headache: methodological issues. Author(s): Service de Neurologie, Hopital Lariboisiere, Paris, France. Source: El Amrani, M Massiou, H Bousser, M G Cephalalgia. 2002 April; 22(3): 205-8 0333-1024
- A retrospective long-term analysis of the epidemiology and features of drug-induced • headache.

Author(s): Department of Neurology, University of Munster, Albert-Schweitzer-Strasse 33, D-48129 Munster, Germany.

Source: Evers, S Suhr, B Bauer, B Grotemeyer, K H Husstedt, I W J-Neurol. 1999 September; 246(9): 802-9 0340-5354

Abnormal 24-hour urinary excretory pattern of 6-sulphatoxymelatonin in both phases • of cluster headache.

Author(s): Neurological Department and Headache Centre, Istituto Nazionale Neurologico C. Besta, Milan, Italy.

Source: Leone, M Lucini, V D'Amico, D Grazzi, L Moschiano, F Fraschini, F Bussone, G Cephalalgia. 1998 December; 18(10): 664-7 0333-1024

- Atlanto-axial subluxation syndrome and management of intractable headache, neck . pain and shoulder pain with auricular stimulation: a clinical case report. Author(s): Kim Institute For Rehabilitation Medicine, Livingston, New Jersey USA. Source: Kim, K H Acupunct-Electrother-Res. 2001; 26(4): 263-75 0360-1293
- Baclofen in cluster headache. Author(s): Department of Neurology, Meir General Hospital, Kfar Saba, and the Sackler Faculty of Medicine, Tel Aviv University, Israel. Source: Hering Hanit, R Gadoth, N Headache. 2000 January; 40(1): 48-51 0017-8748
- Behavioral response to headache: a comparison between migraine and tension-type • headache.

Author(s): Department of Neurology, Hospital de Santa Maria, Lisbon, Portugal. Source: Martins, I P Parreira, E Headache. 2001 June; 41(6): 546-53 0017-8748

- Behavioral self-management in an inpatient headache treatment unit: increasing • adherence and relationship to changes in affective distress. Author(s): Head Pain Treatment Unit at Chelsea Community Hospital, Michigan, USA. Source: Hoodin, F Brines, B J Lake, A E Wilson, J Saper, J R Headache. 2000 May; 40(5): 377-83 0017-8748
- Chronic daily headache. Author(s): Department of Neurology, Hospital Clinico Universitario, University of Valencia, Avda. Blasco Ibanez 17, Valencia 46010, Spain. jlaineza@meditex.es Source: Lainez, M J Monzon, M J Curr-Neurol-Neurosci-Repage 2001 March; 1(2): 118-24 1528-4042
- Clinical observation on scalp acupuncture treatment in 50 cases of headache. Author(s): Guilin Municipal Hospital of Traditional Chinese Medicine, Guilin 541002, Guangxi Province.

Source: Tang, W J-Tradit-Chin-Med. 2002 September; 22(3): 190-2 0254-6272

Cluster headache and periodic affective illness: common chronobiological features. . Author(s): University Centre for Adaptive Disorders and Headache (UCADH), Section of Pavia I, Italy.

Source: Costa, A Leston, J A Cavallini, A Nappi, G Funct-Neurol. 1998 Jul-September; 13(3): 263-72 0393-5264

- Comparison of intravenous valproate versus intramuscular dihydroergotamine and metoclopramide for acute treatment of migraine headache. Author(s): Western New England Pain and Headache Center, Southwestern Vermont Medical Center, Bennington, VT 05201, USA. Source: Edwards, K R Norton, J Behnke, M Headache. 2001 Nov-December; 41(10): 976-80 0017-8748
- Corticosteroid-induced acute mania during a cluster headache episode. Author(s): Department of Neurology, University of Munster, Munster, Germany. luttmann@uni-muenster.de Source: Luttmann, R J Frese, A Erfurth, A Husstedt, I W Evers, S Cephalalgia. 2001 October; 21(8): 852-4 0333-1024
- Effectiveness of topiramate in the prevention of childhood headaches. Author(s): Division of Neurology, University of Cincinnati, College of Medicine, Cincinnati, Ohio, 45229-3039, USA.
   Source: Hershey, A D Powers, S W Vockell, A L LeCates, S Kabbouche, M Headache. 2002 September; 42(8): 810-8 0017-8748
- Eight years of unexplained headaches (why did the diagnosis take so long?). Author(s): Medical Technology Program, University of Wyoming, Laramie 82071-6751, USA.
   Source: Code, W. Clip, Leb Sci. 2001 Fall: 14(4): 228-22.0804.050X

Source: Gade, W Clin-Lab-Sci. 2001 Fall; 14(4): 228-32 0894-959X

- Food and drink. Red wine headaches. Source: Anonymous Harv-Health-Lett. 2002 June; 27(8): 6 1052-1577
- Gabapentin for the treatment and prophylaxis of cluster headache. Author(s): Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong, China. tabenai@cuhk.edu.hk Source: Tay, B A Ngan Kee, W D Chung, D C Reg-Anesth-Pain-Med. 2001 Jul-August; 26(4): 373-5 1098-7339
- Headaches in children and adolescents: update 2001. Author(s): Department of Pediatric Neurology, The Cleveland Clinic Foundation, OH 44195, USA.

Source: Rothner, A D Semin-Pediatr-Neurol. 2001 March; 8(1): 2-6 1071-9091

Hereditary haemochromatosis in two cousins with cluster headache.
 Author(s): Department of Clinical Neuroscience, Section of Neurology, Norwegian University of Science and Technology, Trondheim, Norway. lars.stovner@medisin.ntnu.no

Source: Stovner, L J Hagen, K Waage, A Bjerve, K S Cephalalgia. 2002 May; 22(4): 317-9 0333-1024

- In search of the ideal treatment for migraine headache. Author(s): School of Public Health, Loma Linda University, CA 92350-0001, USA. Source: Bic, Z Blix, G G Hopp, H P Leslie, F M Med-Hypotheses. 1998 January; 50(1): 1-7 0306-9877
- Indomethacin-responsive headaches in children and adolescents. Author(s): Department of Pediatric Neurology, The Cleveland Clinic Foundation, OH 44195, USA.

Source: Moorjani, B I Rothner, A D Semin-Pediatr-Neurol. 2001 March; 8(1): 40-5 1071-9091

• Intravenous valproate sodium in the treatment of daily headache.

Author(s): Department of Neurology, Washington University, St. Louis, MO 63110, USA.

Source: Schwartz, T H Karpitskiy, V V Sohn, R S Headache. 2002 June; 42(6): 519-22 0017-8748

• **Melatonin as adjunctive therapy in the prophylaxis of cluster headache: a pilot study.** Author(s): Department of Neurology and Neurosurgery, Montreal Neurological Institute, McGill University, Montreal, Canada.

Source: Pringsheim, T Magnoux, E Dobson, C F Hamel, E Aube, M Headache. 2002 September; 42(8): 787-92 0017-8748

• Melatonin in the preventive treatment of chronic cluster headache.

Author(s): Jefferson Headache Center, Department of Neurology, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania 19107, USA. marioperes@yahoo.com Source: Peres, M F Rozen, T D Cephalalgia. 2001 December; 21(10): 993-5 0333-1024

• Melatonin-responsive headache in delayed sleep phase syndrome: preliminary observations.

Author(s): Department of Clinical Pharmacy, Hospital 'de Gelderse Vallei' Ede/Bennekom, The Netherlands.

Source: Nagtegaal, J E Smits, M G Swart, A C Kerkhof, G A van der Meer, Y G Headache. 1998 April; 38(4): 303-7 0017-8748

• Migraine MLT-down: an unusual presentation of migraine in patients with aspartame-triggered headaches.

Author(s): The Headache Institute, St. Lukes-Roosevelt Hospital Center, 1000 Tenth Avenue, Suite 1C10, New York, NY 10019, USA.

Source: Newman, L C Lipton, R B Headache. 2001 October; 41(9): 899-901 0017-8748

- Mindfulness meditation in the control of severe headache. Author(s): Department of Psychiatry, Chang Gung Memorial Hospital, Kaohsiung, Taiwan, ROC.
   Source: Sun, T F Kuo, C C Chiu, N M Chang-Gung-Med-J. 2002 August; 25(8): 538-41
- New treatments in cluster headache. Author(s): Department of Neurology T33, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, USA. RozenT@ccf.org Source: Rozen, Todd D Curr-Neurol-Neurosci-Repage 2002 March; 2(2): 114-21 1528-4042
- On call. I've been told that vitamins can prevent headaches. Is it true and if so, what should I take?

Source: Simon, H B Harv-Mens-Health-Watch. 1999 December; 4(5): 8 1089-1102

- Prophylaxis of migraine, transformed migraine, and cluster headache with topiramate. Author(s): Houston Headache Clinic, Houston, Texas 77004, USA. Source: Mathew, N T Kailasam, J Meadors, L Headache. 2002 September; 42(8): 796-803 0017-8748
- Serum glucose regulation and headache. Source: Peroutka, Stephen J Headache. 2002 April; 42(4): 303-8 0017-8748

• Survey on the use of complementary and alternative medicine among patients with headache syndromes.

Author(s): University of Witten/Herdecke, Germany. Source: von Peter, S Ting, W Scrivani, S Korkin, E Okvat, H Gross, M Oz, C Balmaceda, C Cephalalgia. 2002 June; 22(5): 395-400 0333-1024

• **Tension headaches and muscle tension: is there a role for magnesium?** Author(s): Department of Physiology and Pharmacology, and The Center for

Cardiovascular and Muscle Research, SUNY Health Science Center at Brooklyn, New York 11203, USA.

Source: Altura, B M Altura, B T Med-Hypotheses. 2001 December; 57(6): 705-13 0306-9877

• Tension-type headache. Author(s): Diamond Headache Clinic, Chic

Author(s): Diamond Headache Clinic, Chicago, Illinois, USA. Source: Diamond, S Clin-Cornerstone. 1999; 1(6): 33-44 1098-3597

- The outcome of treating patients with suspected rebound headache. Author(s): Department of Neurology, Vanderbilt University School of Medicine, Nashville, Tenn., USA. Source: Warner, J S Headache. 2001 Jul-August; 41(7): 685-92 0017-8748
- The therapeutic potential of melatonin in migraines and other headache types. Author(s): j\_gagnier@hotmail.com Source: Gagnier, J J Altern-Med-Revolume 2001 August; 6(4): 383-9 1089-5159
- The use of ibuprofen plus caffeine to treat tension-type headache. Author(s): Diamond Headache Clinic, 467 West Deming Place, Suite 500, Chicago, IL 60614-1726, USA. MACF48@aol.com Source: Diamond, S Freitag, F G Curr-Pain-Headache-Repage 2001 October; 5(5): 472-8 1531-3433
- Treatment of childhood headaches. Author(s): Department of Child Neurology, Cleveland Clinic Foundation, 9500 Euclid Avenue, S-71, Cleveland, OH 44195, USA. guptaa1@ccf.org Source: Gupta, A Rothner, A D Curr-Neurol-Neurosci-Repage 2001 March; 1(2): 144-54 1528-4042
- Treatment of cluster headache with topiramate: effects and side-effects in five patients.

Author(s): Department of Neurology, Klinikum Grosshadern, Ludwig-Maximilians University, Munich, Germany. SFOE@nefo.med.uni-muenchen.de

Source: Forderreuther, S Mayer, M Straube, A Cephalalgia. 2002 April; 22(3): 186-9 0333-1024

• Trigeminal neuralgic-type pain and vascular-type headache due to gustatory stimulus.

Author(s): Department of Oral Diagnosis, Oral Medicine and Oral Radiology, Hebrew University, Hadassah School of Dental Medicine, Jerusalem, Israel.

Source: Helcer, M Schnarch, A Benoliel, R Sharav, Y Headache. 1998 February; 38(2): 129-31 0017-8748

• Wilfred Harris' early description of cluster headache.

Author(s): Department of Neurology, Mayo Clinic, Rochester, MN 55905, USA. boes.christopher@mayo.edu

Source: Boes, C J Capobianco, D J Matharu, M S Goadsby, P J Cephalalgia. 2002 May; 22(4): 320-6 0333-1024

## **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<sup>®</sup>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 headache; 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: Integrative Medicine Communications; www.drkoop.com

Niacin

Source: Integrative Medicine Communications; www.drkoop.com

#### Niacin

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,892,00.html

#### Riboflavin

Source: Integrative Medicine Communications; www.drkoop.com

Vitamin A Source: Healthnotes, Inc.; www.healthnotes.com

Vitamin A Source: Prima Communications, Inc.www.personalhealthzone.com

Vitamin B2 Source: Healthnotes, Inc.; www.healthnotes.com

#### Vitamin B2

Source: Prima Communications, Inc.www.personalhealthzone.com

### Vitamin B2 (riboflavin)

Source: Integrative Medicine Communications; www.drkoop.com

Vitamin B3

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

#### Vitamin B3

Source: Prima Communications, Inc.www.personalhealthzone.com

Vitamin B3 (niacin) Source: Integrative Medicine Communications; www.drkoop.com

### Vitamin B9 (folic Acid)

Alternative names: Folate, Folic Acid Source: Integrative Medicine Communications; www.drkoop.com

#### Vitamin C

Source: Prima Communications, Inc.www.personalhealthzone.com

#### 92 Headache

#### Vitamin D

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

#### • Minerals

**Calcium** Source: Healthnotes, Inc.; www.healthnotes.com

#### Calcium

Source: Integrative Medicine Communications; www.drkoop.com

## Calcium

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Calcium

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,884,00.html

## **Calcium-channel Blockers**

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

#### Chromium

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Chromium

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10018,00.html

#### Copper

Source: Integrative Medicine Communications; www.drkoop.com

#### Fluoxetine

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

## Folate

Source: Integrative Medicine Communications; www.drkoop.com

#### Folate

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Iodine

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,888,00.html

#### Magnesium

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

#### Magnesium

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Magnesium

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,890,00.html

### Paroxetine

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

#### Retinol

Source: Integrative Medicine Communications; www.drkoop.com

#### Sulfur

Source: Integrative Medicine Communications; www.drkoop.com

### Vitamin a (retinol)

Source: Integrative Medicine Communications; www.drkoop.com

### Zinc

Source: Integrative Medicine Communications; www.drkoop.com

### Zinc

Source: Prima Communications, Inc.www.personalhealthzone.com

#### • Food and Diet

#### Beets

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/foods\_view/0,1523,10,00.html

#### **Fasting Diet**

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

#### Garlic

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Hypoglycemia

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

### Low-salt Diet

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

#### Nutritional Yeast

Alternative names: Brewer's Yeast Source: Integrative Medicine Communications; www.drkoop.com

**Omega-3 Fatty Acids** Source: Integrative Medicine Communications; www.drkoop.com

## **Omega-6 Fatty Acids** Source: Integrative Medicine Communications; www.drkoop.com

## **Tyramine-free Diet**

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

# **CHAPTER 3. ALTERNATIVE MEDICINE AND HEADACHE**

## Overview

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

## The Combined Health Information Database

The Combined Health Information Database (CHID) is a bibliographic database produced by health-related agencies of the U.S. federal government (mostly from the National Institutes of Health) that can offer concise information for a targeted search. The CHID database is updated four times a year at the end of January, April, July, and October. Check the titles, summaries, and availability of CAM-related information by using the "Simple Search" option at the following Web site: http://chid.nih.gov/simple/simple.html. In the drop box at the top, select "Complementary and Alternative Medicine." Then type "headache" (or synonyms) in the second search box. We recommend that you select 100 "documents per page" and to check the "whole records" options. The following was extracted using this technique:

### • Use of Aromatherapy as a Complementary Treatment for Chronic Pain

Source: Alternative Therapies in Health and Medicine. 5(5): 42-51. September 1999.

Summary: This article discusses the use of aromatherapy as a complementary treatment for chronic pain. First, it defines aromatherapy, reviews the effects of aroma on the body, and describes methods of using aromatherapy with and without touch. Then, it summarizes human studies on the use of aromatherapy in the treatment of pain, including aromatherapy for children, lavender for pain and coping, chamomile for pain in cancer, marigold for pain in hyperkeratotic plantar lesions, peppermint for **headache** and arthritic pain, and rose for pain in cancer with bone metastases. Finally, it reviews animal studies, and discusses the potential for untoward effects. It includes a list of essential oils with analgesic properties that are safe to use. The article has 4 tables and 96 references.

## • NIH Consensus Conference: Acupuncture

Source: JAMA. Journal of the American Medical Association. 280(17): 1518-1524. November 4, 1998.

Summary: This journal article presents the findings of the consensus conference on acupuncture, sponsored by the Office of Alternative Medicine and the Office of Medical Applications of Research, National Institutes of Health. The purpose of the conference was to provide clinicians, patients, and the general public with a reliable assessment of the use and effectiveness of acupuncture for a variety of conditions. A multidisciplinary panel evaluated evidence presented by experts and in the scientific literature, and developed a consensus statement addressing five issues: the efficacy of acupuncture compared with placebo or sham acupuncture, the place of acupuncture in clinical practice, the biological effects of acupuncture, the integration of acupuncture into the health care system, and directions for future research. The panel concluded that many of the efficacy studies of acupuncture provide equivocal results because of design, sample size, and other factors. The issue is further complicated by inherent difficulties in the use of appropriate controls. However, promising results have emerged showing the efficacy of acupuncture for adult postoperative and chemotherapy nausea and vomiting, and in postoperative dental pain. In other conditions such as addiction, stroke rehabilitation, headache, menstrual cramps, fibromyalgia, myofascial pain, osteoarthritis, tennis elbow, low back pain, carpal tunnel syndrome, and asthma, acupuncture may be useful as an adjunct treatment, an acceptable alternative, or part of a comprehensive management plan. This article has 66 references.

## 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 headache 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 "headache" (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 headache:

- "Nurse, my head hurts": a review of childhood headaches. Author(s): Kolar KR, Fisher W, Gordon V. Source: J Sch Nurs. 2001 June; 17(3): 120-5. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11885441&dopt=Abstract
- "The moon" and "the blood": two emblematic symbols in headache and epilepsy according to scientific traditions of the Salerno Medical school and popular medicine in southern Italy.
  Author(s): Cassano D, Colucci d'Amato C.
  Source: Journal of the History of the Neurosciences. 1992 April; 1(2): 97-110. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_

uids=11618427&dopt=Abstract

• A cocktail stick is as good as brief acupuncture in episodic tension-type headache (n=50).

Author(s): Cummings M. Source: Acupuncture in Medicine : Journal of the British Medical Acupuncture Society. 2001 June; 19(1): 56-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11471589&dopt=Abstract

- A comparative study on the treatment of migraine headache with combined distant and local acupuncture points versus conventional drug therapy. Author(s): Gao S, Zhao D, Xie Y. Source: Am J Acupunct. 1999; 27(1-2): 27-30. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=10513096&dopt=Abstract
- A comparison of tension headache sufferers and nonpain controls on the State-Trait Anger Expression Inventory: an exploratory study with implications for applied psychophysiologists.

Author(s): Arena JG, Bruno GM, Rozantine GS, Meador KJ. Source: Applied Psychophysiology and Biofeedback. 1997 September; 22(3): 209-14. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=9428970&dopt=Abstract

• A controlled trial of self-help treatment of recurrent headache conducted via the Internet.

Author(s): Strom L, Pettersson R, Andersson G. Source: Journal of Consulting and Clinical Psychology. 2000 August; 68(4): 722-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=10965647&dopt=Abstract

- A pilot study of one-session biofeedback training in pediatric headache. Author(s): Powers SW, Mitchell MJ, Byars KC, Bentti AL, LeCates SL, Hershey AD. Source: Neurology. 2001 January 9; 56(1): 133. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11148256&dopt=Abstract
- A preliminary analysis of EMG variance as an index of change in EMG biofeedback treatment of tension-type headache. Author(s): Rokicki LA, Houle TT, Dhingra LK, Weinland SR, Urban AM, Bhalla RK. Source: Applied Psychophysiology and Biofeedback. 2003 September; 28(3): 205-15.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12964452&dopt=Abstract

• A proposed etiology of cervicogenic headache: the neurophysiologic basis and anatomic relationship between the dura mater and the rectus posterior capitis minor muscle.

Author(s): Alix ME, Bates DK.

### 98 Headache

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Source: Journal of Manipulative and Physiological Therapeutics. 1999 October; 22(8): 534-9. Review.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=10543584&dopt=Abstract

• A randomized controlled trial of exercise and manipulative therapy for cervicogenic headache.

Author(s): Jull G, Trott P, Potter H, Zito G, Niere K, Shirley D, Emberson J, Marschner I, Richardson C.

Source: Spine. 2002 September 1; 27(17): 1835-43; Discussion 1843. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12221344&dopt=Abstract

- A review of the treatment of primary headaches. Part II: Tension-type headache. Author(s): D'Amico D, Grazzi L, Leone M, Moschiano F, Bussone G. Source: Italian Journal of Neurological Sciences. 1998 February; 19(1): 2-9. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=10935852&dopt=Abstract
- Acupuncture for episodic tension-type headache: a multicentre randomized controlled trial.

Author(s): White AR, Resch KL, Chan JC, Norris CD, Modi SK, Patel JN, Ernst E. Source: Cephalalgia : an International Journal of Headache. 2000 September; 20(7): 632-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11128820&dopt=Abstract

- Acupuncture for idiopathic headache. Author(s): Melchart D, Linde K, Fischer P, Berman B, White A, Vickers A, Allais G. Source: Cochrane Database Syst Rev. 2001; (1): Cd001218. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11279710&dopt=Abstract
- Acupuncture for migraine and headache in primary care: a protocol for a pragmatic, randomized trial.

Author(s): Vickers A, Rees R, Zollman C, Smith C, Ellis N. Source: Complementary Therapies in Medicine. 1999 March; 7(1): 3-18. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=10361566&dopt=Abstract

 Acupuncture for recurrent headaches: a systematic review of randomized controlled trials. Author(s): Melchart D, Linde K, Fischer P, White A, Allais G, Vickers A, Berman B. Source: Cephalalgia : an International Journal of Headache. 1999 November; 19(9): 779-86; Discussion 765. Erratum In: Cephalalgia 2000 October; 20(8): 762-3. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_

• Acupuncture in headache. Author(s): Lundeberg T.

uids=10595286&dopt=Abstract

Source: Cephalalgia : an International Journal of Headache. 1999 December; 19 Suppl 25: 65-8. Review.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=10668127&dopt=Abstract

- Acupuncture in headache: a critical review. Author(s): Manias P, Tagaris G, Karageorgiou K. Source: The Clinical Journal of Pain. 2000 December; 16(4): 334-9. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11153790&dopt=Abstract
- Acupuncture in the management of myofascial pain and headache. Author(s): Audette JF, Blinder RA. Source: Current Pain and Headache Reports. 2003 October; 7(5): 395-401. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12946294&dopt=Abstract
- Acupuncture Randomized Trials (ART) in patients with migraine or tension-type headache design and protocols. Author(s): Melchart D, Linde K, Streng A, Reitmayr S, Hoppe A, Brinkhaus B, Becker-Witt C, Wagenpfeil S, Pfaffenrath V, Hammes M, Willich SN, Weidenhammer W. Source: Forschende Komplementarmedizin Und Klassische Naturheilkunde = Research in Complementary and Natural Classical Medicine. 2003 August; 10(4): 179-84. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12972722&dopt=Abstract
- Age comparisons in acquiring biofeedback control and success in reducing headache pain.

Author(s): Sarafino EP, Goehring P. Source: Annals of Behavioral Medicine : a Publication of the Society of Behavioral Medicine. 2000 Winter; 22(1): 10-6. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=10892524&dopt=Abstract

- Alternative Therapies for Headache. Author(s): Young WB, Pozo-Rosich P, Paolone MF. Source: Current Treatment Options in Neurology. 2003 November; 5(6): 441-553. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=14516522&dopt=Abstract
- Alternative therapies in headache. Is there a role? Author(s): Mauskop A. Source: The Medical Clinics of North America. 2001 July; 85(4): 1077-84. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11480259&dopt=Abstract
- An exploratory study of reflexological treatment for headache. Author(s): Launso L, Brendstrup E, Arnberg S.
Source: Alternative Therapies in Health and Medicine. 1999 May; 5(3): 57-65. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=10234869&dopt=Abstract

• Atlanto-axial subluxation syndrome and management of intractable headache, neck pain and shoulder pain with auricular stimulation: a clinical case report. Author(s): Kim KH.

Source: Acupuncture & Electro-Therapeutics Research. 2001; 26(4): 263-75. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=11841111&dopt=Abstract

 Behavioral and nonpharmacologic treatments of headache. Author(s): Lake AE 3rd.
 Source: The Medical Clinics of North America. 2001 July; 85(4): 1055-75. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=11480258&dopt=Abstract

• Behavioral management of recurrent headache: three decades of experience and empiricism.

Author(s): Penzien DB, Rains JC, Andrasik F. Source: Applied Psychophysiology and Biofeedback. 2002 June; 27(2): 163-81. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12206049&dopt=Abstract

• Behavioral response to headache: a comparison between migraine and tension-type headache.

Author(s): Martins IP, Parreira E. Source: Headache. 2001 June; 41(6): 546-53. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11437889&dopt=Abstract

- Behavioral self-management in an inpatient headache treatment unit: increasing adherence and relationship to changes in affective distress. Author(s): Hoodin F, Brines BJ, Lake AE 3rd, Wilson J, Saper JR. Source: Headache. 2000 May; 40(5): 377-83. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=10849032&dopt=Abstract
- Behavioral treatment approaches to chronic headache. Author(s): Andrasik F. Source: Neurological Sciences : Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology. 2003 May; 24 Suppl 2: S80-5. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12811599&dopt=Abstract
- Benign hot bath-related headache. Author(s): Negoro K, Morimatsu M, Ikuta N, Nogaki H.

Source: Headache. 2000 February; 40(2): 173-5. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=10759919&dopt=Abstract

- Biofeedback in the treatment of headache and other childhood pain. Author(s): Hermann C, Blanchard EB. Source: Applied Psychophysiology and Biofeedback. 2002 June; 27(2): 143-62. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12206048&dopt=Abstract
- Biofeedback-assisted relaxation in migraine headache: relationship to cerebral blood flow velocity in the middle cerebral artery. Author(s): Vasudeva S, Claggett AL, Tietjen GE, McGrady AV. Source: Headache. 2003 March; 43(3): 245-50. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12603643&dopt=Abstract
- Biofeedback-assisted relaxation training for young adolescents with tension-type headache: a controlled study.

Author(s): Bussone G, Grazzi L, D'Amico D, Leone M, Andrasik F. Source: Cephalalgia : an International Journal of Headache. 1998 September; 18(7): 463-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=9793698&dopt=Abstract

• Breath-holding, head pressure, and hot water: an effective treatment for migraine headache.

Author(s): Schulman EA. Source: Headache. 2002 November-December; 42(10): 1048-50. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12453039&dopt=Abstract

- Brief cognitive-behavioral group treatment for children's headache. Author(s): Barry J, von Baeyer CL. Source: The Clinical Journal of Pain. 1997 September; 13(3): 215-20. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=9303253&dopt=Abstract
- Calcitonin gene-related Peptide in tension-type headache. Author(s): Ashina M.
   Source: Scientificworldjournal. 2001 December 18; 1(12 Suppl 1): 30. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=14532404&dopt=Abstract
- Calcitonin gene-related Peptide in tension-type headache. Author(s): Ashina M. Source: Scientificworldjournal. 2002 June 7; 2(6): 1527-31. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12806133&dopt=Abstract

- Capsaicin stimulation of the cochlea and electric stimulation of the trigeminal ganglion mediate vascular permeability in cochlear and vertebro-basilar arteries: a potential cause of inner ear dysfunction in headache. Author(s): Vass Z, Steyger PS, Hordichok AJ, Trune DR, Jancso G, Nuttall AL. Source: Neuroscience. 2001; 103(1): 189-201. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=11311800&dopt=Abstract
- Central sensitization in tension-type headache--possible pathophysiological mechanisms.

Author(s): Bendtsen L. Source: Cephalalgia : an International Journal of Headache. 2000 June; 20(5): 486-508. Review.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=11037746&dopt=Abstract

• Cervicogenic headache: manual and manipulative therapies. Author(s): Grimshaw DN.

Source: Current Pain and Headache Reports. 2001 August; 5(4): 369-75. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11403741&dopt=Abstract

• Cervicogenic headache: mechanisms, evaluation, and treatment strategies. Author(s): Biondi DM.

Source: J Am Osteopath Assoc. 2000 September; 100(9 Suppl): S7-14. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=11070659&dopt=Abstract

# • Cervicogenic headaches: a critical review.

Author(s): Haldeman S, Dagenais S. Source: The Spine Journal : Official Journal of the North American Spine Society. 2001 January-February; 1(1): 31-46. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=14588366&dopt=Abstract

• Childhood migraine headache syndromes.

Author(s): Prensky A. Source: Current Treatment Options in Neurology. 2001 May; 3(3): 257-270. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11282041&dopt=Abstract

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Author(s): Lainez MJ, Monzon MJ. Source: Curr Neurol Neurosci Rep. 2001 March; 1(2): 118-24. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11898507&dopt=Abstract

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- Chronic nonprogressive headaches in children and adolescents. Author(s): Jensen VK, Rothner AD. Source: Semin Pediatr Neurol. 1995 June; 2(2): 151-8. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=9422242&dopt=Abstract
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- Clinical microbiological case: fever and headache in a heavy consumer of eucalyptus extract.

Author(s): Tascini C, Ferranti S, Gemignani G, Messina F, Menichetti F. Source: Clinical Microbiology and Infection : the Official Publication of the European Society of Clinical Microbiology and Infectious Diseases. 2002 July; 8(7): 437, 445-6. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12199856&dopt=Abstract

• Clinical observation on scalp acupuncture treatment in 50 cases of headache. Author(s): Tang W.

Source: J Tradit Chin Med. 2002 September; 22(3): 190-2. No Abstract Available. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12400424&dopt=Abstract

- Cluster headache: imaging and other developments. Author(s): May A, Goadsby PJ. Source: Current Opinion in Neurology. 1998 June; 11(3): 199-203. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=9642536&dopt=Abstract
- Cognitive-behavioral issues in the treatment and management of chronic daily headache.

Author(s): Lipchik GL, Nash JM.

Source: Current Pain and Headache Reports. 2002 December; 6(6): 473-9. Review. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12413406&dopt=Abstract

• Cognitive-behavioral therapy of pediatric headache: are there differences in efficacy between a therapist-administered group training and a self-help format? Author(s): Kroener-Herwig B, Denecke H.

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Source: Journal of Psychosomatic Research. 2002 December; 53(6): 1107-14. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12479993&dopt=Abstract

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Author(s): Ramadan NM.

Source: Applied Psychophysiology and Biofeedback. 2001 December; 26(4): 325-7; Discussion 329-30.

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=11802681&dopt=Abstract

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- Cranial electrostimulation for headache: meta-analysis. Author(s): McCrory DC. Source: The Journal of Nervous and Mental Disease. 1997 December; 185(12): 766-7. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=9442190&dopt=Abstract
- Debate: homeopathy and chronic headache.

Author(s): Oberbaum M. Source: Homeopathy. 2002 July; 91(3): 188-9; Author Reply 189-90. No Abstract Available. http://www.pcbi.plm.pib.gov;80/entrez/guery.fcgi2cmd=Retrieve&db=PubMed&list

http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12322875&dopt=Abstract

- Debate: homeopathy and chronic headache.
  Author(s): Vithoulkas G.
  Source: Homeopathy. 2002 July; 91(3): 186-8; Author Reply 189-90. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12322874&dopt=Abstract
- Direction of temperature control in the thermal biofeedback treatment of vascular headache.

Author(s): Blanchard EB, Peters ML, Hermann C, Turner SM, Buckley TC, Barton K, Dentinger MP.

Source: Applied Psychophysiology and Biofeedback. 1997 December; 22(4): 227-45. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=9595177&dopt=Abstract

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# headache?

Author(s): Wylie KR, Jackson C, Crawford PM. Source: J Tradit Chin Med. 1997 June; 17(2): 130-9. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=10437184&dopt=Abstract

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Author(s): Fichtel A, Larsson B. Source: Headache. 2001 March; 41(3): 290-6. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11264690&dopt=Abstract

• Drug-induced headache: long-term results of stationary versus ambulatory withdrawal therapy.

Author(s): Suhr B, Evers S, Bauer B, Gralow I, Grotemeyer KH, Husstedt IW. Source: Cephalalgia : an International Journal of Headache. 1999 January; 19(1): 44-9. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=10099859&dopt=Abstract

- Effect of autogenic training on drug consumption in patients with primary headache: an 8-month follow-up study.
   Author(s): Zsombok T, Juhasz G, Budavari A, Vitrai J, Bagdy G.
   Source: Headache. 2003 March; 43(3): 251-7.
   http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=12603644&dopt=Abstract
- Effect of guided imagery on quality of life for patients with chronic tension-type headache.

Author(s): Mannix LK, Chandurkar RS, Rybicki LA, Tusek DL, Solomon GD. Source: Headache. 1999 May; 39(5): 326-34. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11279912&dopt=Abstract

• Efficacy and effect of SI17 therapy on pancreatic polypeptide in vascular and tensiontype headache.

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   Source: Journal of Manipulative and Physiological Therapeutics. 1999 March-April; 22(3): 166-70. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=10220716&dopt=Abstract
- Use of percutaneous electrical nerve stimulation (PENS) for treating ECT-induced headaches.

Author(s): Ghoname EA, Craig WF, White PF. Source: Headache. 1999 July-August; 39(7): 502-5. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_ uids=11279935&dopt=Abstract

- Use of percutaneous electrical nerve stimulation (PENS) in the short-term management of headache. Author(s): Ahmed HE, White PF, Craig WF, Hamza MA, Ghoname ES, Gajraj NM. Source: Headache. 2000 April; 40(4): 311-5. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=10759936&dopt=Abstract
- Vectored upper cervical manipulation for chronic sleep bruxism, headache, and cervical spine pain in a child. Author(s): Knutson GA.
   Source: Journal of Manipulative and Physiological Therapeutics. 2003 July-August; 26(6): E16. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12902973&dopt=Abstract
- Your headache is a cow. Author(s): Evans RW, Penzien DB.

Source: Headache. 2003 February; 43(2): 168-9. http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\_uids=12558773&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<sup>®</sup>: 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<sup>®</sup>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 headache; 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

### AIDS and HIV

Source: Integrative Medicine Communications; www.drkoop.com

# Alcohol Withdrawal

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

# Alcoholism

Source: Integrative Medicine Communications; www.drkoop.com

# **Allergic Rhinitis**

Source: Integrative Medicine Communications; www.drkoop.com

#### 118 Headache

Allergies and Sensitivities Source: Healthnotes, Inc.; www.healthnotes.com

### Alzheimer's Disease

Source: Integrative Medicine Communications; www.drkoop.com

#### Amenorrhea

Source: Integrative Medicine Communications; www.drkoop.com

#### Anaphylaxis

Source: Integrative Medicine Communications; www.drkoop.com

#### Anemia

Source: Integrative Medicine Communications; www.drkoop.com

### Angina

Source: Integrative Medicine Communications; www.drkoop.com

#### Asthma

Source: Integrative Medicine Communications; www.drkoop.com

#### **Bone Marrow Disorders**

Source: Integrative Medicine Communications; www.drkoop.com

#### Brain Cancer

Source: Integrative Medicine Communications; www.drkoop.com

### Breast Cancer

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

#### **Chickenpox and Shingles**

Source: Integrative Medicine Communications; www.drkoop.com

#### Chronic Candidiasis Source: Healthnotes, Inc.; www.healthnotes.com

Chronic Fatigue Syndrome Source: Integrative Medicine Communications; www.drkoop.com

# Chronic Myelogenous Leukemia

Source: Integrative Medicine Communications; www.drkoop.com

# **Cluster Headache**

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

#### **Colds and Flus**

Source: Prima Communications, Inc.www.personalhealthzone.com

#### **Colorectal Cancer**

Source: Integrative Medicine Communications; www.drkoop.com

**Common Cold** Source: Integrative Medicine Communications; www.drkoop.com

**Congestive Heart Failure** Source: Integrative Medicine Communications; www.drkoop.com

**Cyclic Mastalgia** Alternative names: Cyclic Mastitis, Fibrocystic Breast Disease Source: Prima Communications, Inc.www.personalhealthzone.com

**Depression (Mild to Moderate)** Source: Prima Communications, Inc.www.personalhealthzone.com

**Diabetes** Source: Prima Communications, Inc.www.personalhealthzone.com

**Dysmenorrhea** Source: Healthnotes, Inc.; www.healthnotes.com

**Dysmenorrhea** Source: Integrative Medicine Communications; www.drkoop.com

Endocarditis Source: Integrative Medicine Communications; www.drkoop.com

**Epilepsy** Source: Healthnotes, Inc.; www.healthnotes.com

**Epilepsy** Source: Integrative Medicine Communications; www.drkoop.com

**Epstein-Barr Virus** Source: Integrative Medicine Communications; www.drkoop.com

**Fainting** Source: Integrative Medicine Communications; www.drkoop.com

**Fibromyalgia** Source: Integrative Medicine Communications; www.drkoop.com

Flu

Source: Integrative Medicine Communications; www.drkoop.com

**Food Allergy** Source: Integrative Medicine Communications; www.drkoop.com

**Food Poisoning** Source: Integrative Medicine Communications; www.drkoop.com

Frostbite Source: Integrative Medicine Communications; www.drkoop.com **Gestational Hypertension** Source: Healthnotes, Inc.; www.healthnotes.com

Hay Fever Source: Healthnotes, Inc.; www.healthnotes.com

Hay Fever Source: Integrative Medicine Communications; www.drkoop.com

Heat Exhaustion Source: Integrative Medicine Communications; www.drkoop.com

Herpes Zoster and Varicella Viruses Source: Integrative Medicine Communications; www.drkoop.com

High Blood Pressure Source: Integrative Medicine Communications; www.drkoop.com

High Cholesterol Source: Healthnotes, Inc.; www.healthnotes.com

High Cholesterol Source: Integrative Medicine Communications; www.drkoop.com

High Cholesterol Source: Prima Communications, Inc.www.personalhealthzone.com

Histoplasmosis Source: Integrative Medicine Communications; www.drkoop.com

Hiv and Aids Source: Integrative Medicine Communications; www.drkoop.com

**Hypercholesterolemia** Source: Integrative Medicine Communications; www.drkoop.com

**Hypertension** Source: Healthnotes, Inc.; www.healthnotes.com

**Hypertension** Source: Integrative Medicine Communications; www.drkoop.com

**Hypoglycemia** Source: Integrative Medicine Communications; www.drkoop.com

**Hypoparathyroidism** Source: Integrative Medicine Communications; www.drkoop.com

**Hypothyroidism** Source: Integrative Medicine Communications; www.drkoop.com Influenza Source: Healthnotes, Inc.; www.healthnotes.com

#### Influenza

Source: Integrative Medicine Communications; www.drkoop.com

#### Insomnia

Source: Prima Communications, Inc.www.personalhealthzone.com

#### **Intestinal Parasites**

Source: Integrative Medicine Communications; www.drkoop.com

#### **Iron-Deficiency Anemia**

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

#### Jet Lag

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

#### Low Blood Sugar

Source: Integrative Medicine Communications; www.drkoop.com

#### Lung Cancer

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

#### Lupus

Source: Integrative Medicine Communications; www.drkoop.com

#### Lyme Disease

Source: Integrative Medicine Communications; www.drkoop.com

#### Meningitis

Source: Integrative Medicine Communications; www.drkoop.com

#### Menopause

Source: Integrative Medicine Communications; www.drkoop.com

#### Menstrual Pain

Source: Integrative Medicine Communications; www.drkoop.com

# Migraine Headache

Source: Integrative Medicine Communications; www.drkoop.com

### **Migraine Headaches**

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

#### **Migraine Headaches**

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Mononucleosis

Source: Integrative Medicine Communications; www.drkoop.com

#### 122 Headache

Motion Sickness Source: Healthnotes, Inc.; www.healthnotes.com

**Motion Sickness** Source: Integrative Medicine Communications; www.drkoop.com

MSG Sensitivity Source: Healthnotes, Inc.; www.healthnotes.com

#### Mumps

Source: Integrative Medicine Communications; www.drkoop.com

#### **Myelofibrosis**

Source: Integrative Medicine Communications; www.drkoop.com

### **Myeloproliferative Disorders**

Source: Integrative Medicine Communications; www.drkoop.com

Pain

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

### Photodermatitis

Source: Integrative Medicine Communications; www.drkoop.com

#### PMS

Source: Integrative Medicine Communications; www.drkoop.com

#### PMS

Alternative names: Premenstrual Stress Syndrome Source: Prima Communications, Inc.www.personalhealthzone.com

Polycythemia Vera

Source: Integrative Medicine Communications; www.drkoop.com

# Preeclampsia

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

**Premenstrual Syndrome** Source: Healthnotes, Inc.; www.healthnotes.com

**Premenstrual Syndrome** Source: Integrative Medicine Communications; www.drkoop.com

**Radiation Damage** Source: Integrative Medicine Communications; www.drkoop.com

**Raynaud's Phenomenon** Source: Integrative Medicine Communications; www.drkoop.com

#### Rubella

Source: Integrative Medicine Communications; www.drkoop.com

Seasonal Affective Disorder Source: Healthnotes, Inc.; www.healthnotes.com

Seizure Disorders Source: Integrative Medicine Communications; www.drkoop.com

Shingles and Chickenpox Source: Integrative Medicine Communications; www.drkoop.com

Sinus Headache Source: Integrative Medicine Communications; www.drkoop.com

Sinus Infection Source: Integrative Medicine Communications; www.drkoop.com

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

Sinusitis Source: Integrative Medicine Communications; www.drkoop.com

Sleep Apnea Source: Integrative Medicine Communications; www.drkoop.com

Sleeplessness Source: Integrative Medicine Communications; www.drkoop.com

**Stroke** Source: Healthnotes, Inc.; www.healthnotes.com

Stroke

Source: Integrative Medicine Communications; www.drkoop.com

Sunburn

Source: Integrative Medicine Communications; www.drkoop.com

**Syncope** Source: Integrative Medicine Communications; www.drkoop.com

**Systemic Lupus Erythematosus** Source: Healthnotes, Inc.; www.healthnotes.com

**Systemic Lupus Erythematosus** Source: Integrative Medicine Communications; www.drkoop.com

**Temporomandibular Joint Dysfunction** Source: Integrative Medicine Communications; www.drkoop.com

Tension Headache Source: Healthnotes, Inc.; www.healthnotes.com

#### 124 Headache

#### **Tension Headache**

Source: Integrative Medicine Communications; www.drkoop.com

#### Thrombocytosis

Source: Integrative Medicine Communications; www.drkoop.com

#### TIAs

Source: Integrative Medicine Communications; www.drkoop.com

#### TMJ

Source: Integrative Medicine Communications; www.drkoop.com

#### Transient Ischemic Attacks

Source: Integrative Medicine Communications; www.drkoop.com

#### Tuberculosis

Source: Integrative Medicine Communications; www.drkoop.com

# Varicella and Herpes Zoster Viruses

Source: Integrative Medicine Communications; www.drkoop.com

# Varicose Veins

Source: Prima Communications, Inc.www.personalhealthzone.com

**Vertigo** Source: Healthnotes, Inc.; www.healthnotes.com

#### Wilson's Disease Source: Healthnotes, Inc.; www.healthnotes.com

#### • Alternative Therapy

#### Acupressure

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,662,00.html

#### Acupuncture

Source: Integrative Medicine Communications; www.drkoop.com

#### Acupuncture

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,663,00.html

#### Aston-patterning

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10118,00.html

## **Bach Flower Remedies**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com

Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,673,00.html

### Biofeedback

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

### Biofeedback

Source: Integrative Medicine Communications; www.drkoop.com

### Biofeedback

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,675,00.html

### Chiropractic

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

### Chiropractic

Source: Integrative Medicine Communications; www.drkoop.com

### Chiropractic

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,681,00.html

### **Colon Therapy**

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

# **Colon Therapy**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,682,00.html

# **Craniosacral Therapy**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,685,00.html

# **Crystal Healing**

Alternative names: crystal therapeutics crystal therapy crystal work Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D. Hyperlink: http://www.canoe.ca/AltmedDictionary/c.html

### **Detoxification Therapy**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10119,00.html

### Fasting

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com

Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,694,00.html

# Feldenkrais

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,695,00.html

# **Guided Imagery**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,699,00.html

# Herbal Medicine

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

# Hydrotherapy

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,705,00.html

# Hypnotherapy

Source: Integrative Medicine Communications; www.drkoop.com

# Light Therapy

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,713,00.html

# **Magnet Therapy**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,715,00.html

# Meditation

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,717,00.html

# **Music Therapy**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,719,00.html

# Myotherapy

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,931,00.html

# Naturopathy

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com

Hyperlink:

http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,722,00.html

### Osteopathy

Source: Integrative Medicine Communications; www.drkoop.com

### Osteopathy

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,724,00.html

### **Polarity Therapy**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,727,00.html

### Reflexology

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,730,00.html

### **Relaxation Techniques**

Source: Integrative Medicine Communications; www.drkoop.com

# Rolfing

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,732,00.html

### Shiatsu

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,733,00.html

# Tai Chi

Source: Integrative Medicine Communications; www.drkoop.com

### Therapeutic Touch

Source: Integrative Medicine Communications; www.drkoop.com

# **Therapeutic Touch**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,739,00.html

### **Traditional Chinese Medicine**

Source: Integrative Medicine Communications; www.drkoop.com

# **Traditional Chinese Medicine**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10085,00.html

# **Trager Approach**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,741,00.html

### Yoga

Source: Integrative Medicine Communications; www.drkoop.com

# • Chinese Medicine

### Baifuzi

Alternative names: Giant Typhonium Rhizome; Rhizoma Typhonii Source: Chinese Materia Medica

### Baishao

Alternative names: White Peony Root; Radix Paeoniae Alba Source: Chinese Materia Medica

### Baizhi

Alternative names: Dahurian Angelica Root; Radix Angelicae Dahuricae Source: Chinese Materia Medica

# Banxia

Alternative names: Pinellia Tuber; Rhizoma Pinelliae Source: Chinese Materia Medica

# **Baokening Keli**

Alternative names: Baokening Granules Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China Hyperlink: http://www.newcenturynutrition.com/cgilocal/patent\_herbs\_db/db.cgi?db=default&Chinese=Baokening%20Keli&mh=10&s b=---&view\_records=View+Records

# **Biwen San**

Alternative names: Biwen Powder Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

# Bohe

Alternative names: Peppermint; Herba Menthae Source: Chinese Materia Medica

# Cang'erzi

Alternative names: Siberian Cocklebur Fruit; Fructus Xanthii Source: Chinese Materia Medica

#### Caowu

Alternative names: Kusnezoff Monkshood Leaf; Caowuye; Folium Aconiti Kusnezoffii Source: Chinese Materia Medica

#### Caowuye

Alternative names: Kusnezoff Monkshood Leaf; Folium Aconiti Kusnezoffii Source: Chinese Materia Medica

#### Chongweizi

Alternative names: Motherwort Fruit; Fructus Leonuri Source: Chinese Materia Medica

#### Chuanxion

Alternative names: Chuanxiong Chatiao Pills; Chuanxiong Chatiao Wan Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

#### Chuanxiong

Alternative names: Szechwan Lovage Rhizome; Rhizoma Chuanxiong Source: Chinese Materia Medica

#### **Chuanxiong Chatiao San**

Alternative names: Chuanxiong Chatiao Powder Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

### **Cuitang Wan**

Alternative names: Cuitang Pills Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

### Dahuang Qingwei Wan

Alternative names: Dahuang Qingwei Pills Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

#### Dandouchi

Alternative names: Fermented Soybean; Semen Sojae Preparatum Source: Chinese Materia Medica

#### Duhuo

Alternative names: Doubleteeth Pubescent Angelica Root; Radix Angelicae Pubescentis Source: Chinese Materia Medica

### Ebushicao

Alternative names: Small Centipeda Herb; Herba Centipedae Source: Chinese Materia Medica

#### Fabanxia

Alternative names: Prepared Pinellia Tuber; Rhizoma Pinelliae Preparata Source: Chinese Materia Medica

#### Fangfeng

Alternative names: Divaricate Saposhnikovia Root; Radix Saposhnikoviae Source: Chinese Materia Medica

#### Fangfeng Tongsheng Wan

Alternative names: Fangfeng Tongsheng Pills Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

#### Fuzi

Alternative names: Beivedere Fruit; Difuzi; Fructus Kochiae Source: Chinese Materia Medica

#### Ganmao Qingre Keli

Alternative names: Ganmao Qingre Granules Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

### Gegen

Alternative names: Kudzuvine Root; Radix Puerariae Source: Chinese Materia Medica

#### Gouteng

Alternative names: Gambir Plant; Ramulus Uncariae cum Uncis Source: Chinese Materia Medica

#### Guanghuoxiang

Alternative names: Cablin Patchouli Herb; Herba Pogostemonis Source: Chinese Materia Medica

#### Gujingcao

Alternative names: Pipewort Flower; Flos Eriocauli Source: Chinese Materia Medica **Huaihua** Alternative names: Pagodatree Flower; Flos Sophorae Source: Chinese Materia Medica

### Huodan Wan

Alternative names: Huodan Pills Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

### Huoxiang Zhengqi Shui

Alternative names: Huoxiang Zhengqi Solution Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

# Jili

Alternative names: Puncturevine Caltrop Fruit; Fructus Tribuli Source: Chinese Materia Medica

### Jingjie

Alternative names: Fineleaf Schizonepeta Herb; Herba Schizonepetae Source: Chinese Materia Medica

# Jiuwei Qianghuo Keli

Alternative names: Jiuwei Oianghuo Granules Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

### Jiuwei Qianghuo Wan

Alternative names: Jiuwei Qianghuo Pills Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

### Juemingzi

Alternative names: Cassia Seed; Semen Cassiae Source: Chinese Materia Medica

### Juhua

Alternative names: Chrysanthemum Flower; Flos Chrysanthemi Source: Chinese Materia Medica

### Kanggan Keli

Alternative names: Kanggan Granules Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

### Lingyangjiao

Alternative names: Antelope Horn; Cornu Saigae Tataricae Source: Chinese Materia Medica

# Liuhe Dingzhong Wan

Alternative names: Liuhe Dingzhong Pills Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

### Mahuang

Alternative names: Ephedra; Herba EphedraeHerba Ephedrae Source: Chinese Materia Medica

### Manjingzi

Alternative names: Shrub Chastetree Fruit; Fructus Viticis Source: Chinese Materia Medica

### Muxiang

Alternative names: Slender Dutchmanspipe Root; Qingmuxiang; Radix Aristolochiae Source: Chinese Materia Medica

# Pangdahai

Alternative names: Boat-fruited Sterculia Seed; Semen Sterculiae Lychnophorae Source: Chinese Materia Medica

# Qianghou

Alternative names: Incised Notopterygium Rhizome or Root; Rhizoma seu Radix Notopterygii Source: Chinese Materia Medica

### Qingmuxiang

Alternative names: Slender Dutchmanspipe Root; Radix Aristolochiae Source: Chinese Materia Medica

# Qingxuan Wan

Alternative names: Qingxuan Pills Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

### Qinlian Pian

Alternative names: Gegen Qinlian Tablets; Gegen Qinlian Pian Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

# Qiwei Ketengzi Wan

Alternative names: Qiwei Ketengzi Pills Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

# Quanxie

Alternative names: Scorpion; Scorpio Source: Chinese Materia Medica

### Sangye

Alternative names: Mulberry Leaf; Folium Mori Source: Chinese Materia Medica

# Shengma

Alternative names: Largetrifoliolious Bugbane Rhizome; Rhizoma Cimicifugae Source: Chinese Materia Medica

# Shensu Wan

Alternative names: Shensu Pills; Shensu Wan<br/>shensu Wan<br/>she

# Shigao

Alternative names: Gypsum; Gypsum Fibrosum Source: Chinese Materia Medica

# Shijueming

Alternative names: Sea-ear Shell; Concha Haliotidis Source: Chinese Materia Medica

### Siwei Tumuxiang San

Alternative names: Siwei Tumuxiang Powder; Siwei Tumuxiang San<br/>br>(Si Wei Tu Mu Xiang San) Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

# Tianma

Alternative names: Tall Gastrodia Tuber; Rhizoma Gastrodiae Source: Chinese Materia Medica

### Wuzhuyu

Alternative names: Medicinal Evodia Fruit; Fructus Evodiae Source: Chinese Materia Medica

### Xiakucao

Alternative names: Common Selfheal Fruit-Spike; Spica Prunellae Source: Chinese Materia Medica

# Xiangru

Alternative names: Haichow Elsholtzia Herb; Herba Mosiae Source: Chinese Materia Medica

# Xinyi

Alternative names: Biond Magnolia Flower; Flos Magnoliae Source: Chinese Materia Medica

# Xixin

Alternative names: Manchurian Wildginger; Herba Asari Source: Chinese Materia Medica

# Yejuhua

Alternative names: Wild Chrysanthemum Flower; Flos Chrysanthemi Indici Source: Chinese Materia Medica

# Zhenzhu

Alternative names: Nacre; Zhenzhumu; Concha Margaritifera Usta Source: Chinese Materia Medica

# Zhenzhumu

Alternative names: Nacre; Concha Margaritifera Usta Source: Chinese Materia Medica

# • Herbs and Supplements

5-htp

Source: Integrative Medicine Communications; www.drkoop.com

# 5-htp (5-hydroxytryptophan)

Source: Prima Communications, Inc.www.personalhealthzone.com

# 5-hydroxytryptophan

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

# 5-hydroxytryptophan (5-htp)

Source: Integrative Medicine Communications; www.drkoop.com

### Ala

Source: Integrative Medicine Communications; www.drkoop.com

Alpha-linolenic Acid (ala) Source: Integrative Medicine Communications; www.drkoop.com

### **American Ginseng**

Alternative names: Ginseng, American Source: Integrative Medicine Communications; www.drkoop.com

Amino Acid K Source: Integrative Medicine Communications; www.drkoop.com

Amino Acids Overview Source: Healthnotes, Inc.; www.healthnotes.com

### Aminoglycosides

Source: Integrative Medicine Communications; www.drkoop.com

# Andrographis

Alternative names: Andrographis paniculata Source: Healthnotes, Inc.; www.healthnotes.com

### **Angelica Sinensis**

Source: Integrative Medicine Communications; www.drkoop.com

### Angkak

Source: Integrative Medicine Communications; www.drkoop.com

### Antibiotic Combination: Sulfa Drugs

Source: Integrative Medicine Communications; www.drkoop.com

### Arctium

Alternative names: Burdock, Gobo; Arctium lappa L. Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

# Asian Ginseng

Alternative names: Ginseng, Asian Source: Integrative Medicine Communications; www.drkoop.com

### Ava

Source: Integrative Medicine Communications; www.drkoop.com

**Barbiturates** Source: Healthnotes, Inc.; www.healthnotes.com

#### Barbiturates

Source: Integrative Medicine Communications; www.drkoop.com

#### **Bee Products**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,756,00.html

#### Beni-koji

Source: Integrative Medicine Communications; www.drkoop.com

#### **Beta-adrenergic Blockers**

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

#### Beta-carotene

Source: Prima Communications, Inc.www.personalhealthzone.com

#### **Biguanides**

Source: Integrative Medicine Communications; www.drkoop.com

#### **Bile Acid Sequestrants**

Source: Integrative Medicine Communications; www.drkoop.com

#### **Bitter Melon**

Alternative names: Momordica charantia Source: Healthnotes, Inc.; www.healthnotes.com

#### **Black Cohosh**

Alternative names: Cimicifuga racemosa Source: Healthnotes, Inc.; www.healthnotes.com

#### **Black Cohosh**

Alternative names: Cimicifuga racemosa (actea), Black Snakeroot Source: Integrative Medicine Communications; www.drkoop.com

#### **Black Cohosh**

Source: Prima Communications, Inc.www.personalhealthzone.com

#### **Black Cohosh**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10009,00.html

# **Black Snakeroot**

Source: Integrative Medicine Communications; www.drkoop.com

# **Blue Cohosh**

Alternative names: Caulophyllum thalictroides Source: Healthnotes, Inc.; www.healthnotes.com
## Brahmi

Alternative names: Centella asiatica , Centella, March Pennywort, Indian Pennywort, Hydrocotyle, Brahmi (Sanskrit), Luei Gong Gen (Chinese)(Note: Gotu kola should not be confused with kola nut.) Source: Integrative Medicine Communications; www.drkoop.com

# **Brewer's Yeast**

Alternative names: Nutritional Yeast Source: Integrative Medicine Communications; www.drkoop.com

## Bromelain

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

#### Butalbital

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

#### Caffeine

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

#### **Camellia Sinensis**

Source: Integrative Medicine Communications; www.drkoop.com

#### Caprylic Acid

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10111,00.html

#### Cayenne

Alternative names: Capsicum annuum, Capsicum frutescens Source: Healthnotes, Inc.; www.healthnotes.com

#### Cayenne

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,765,00.html

#### Centella

Source: Integrative Medicine Communications; www.drkoop.com

# Centella Asiatica

Alternative names: Centella asiatica , Centella, March Pennywort, Indian Pennywort, Hydrocotyle, Brahmi (Sanskrit), Luei Gong Gen (Chinese)(Note: Gotu kola should not be confused with kola nut.) Source: Integrative Medicine Communications; www.drkoop.com

#### Cephalosporins

Source: Integrative Medicine Communications; www.drkoop.com

#### Chamomile

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Chasteberry

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Chinese Angelica

Source: Integrative Medicine Communications; www.drkoop.com

#### **Chrysanthemum Parthenium**

Source: Integrative Medicine Communications; www.drkoop.com

#### Cimicifuga Racemosa (actea)

Source: Integrative Medicine Communications; www.drkoop.com

#### Corydalis

Alternative names: Corydalis turtschaninovii, Corydalis yanhusuo Source: Healthnotes, Inc.; www.healthnotes.com

#### Cysteine

Source: Integrative Medicine Communications; www.drkoop.com

#### Dandelion

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Danggui

Alternative names: Angelica sinensis, Chinese Angelica, Dang Gui, Danngui, Dong Qua, Tang Kuei, Tan Kue Bai zhi(Note: Dong quai should not be confused with Angelica root or Angelica seed.) Source: Integrative Medicine Communications; www.drkoop.com

#### Dehydroepiandrosterone (dhea)

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

#### Devil's Claw

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,970,00.html

#### Dmso

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

#### Docosahexaenoic Acid

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

#### Dong Quai

Alternative names: Angelica sinensis, Chinese Angelica, Dang Gui, Danngui, Dong Qua, Tang Kuei, Tan Kue Bai zhi(Note: Dong quai should not be confused with Angelica root or Angelica seed.) Source: Integrative Medicine Communications; www.drkoop.com

#### Echinacea

Source: Prima Communications, Inc.www.personalhealthzone.com

# Electrolytes

Source: Integrative Medicine Communications; www.drkoop.com

# **English Lavendar**

Source: Integrative Medicine Communications; www.drkoop.com

# Ephedra

Alternative names: Ephedra sinica, Ephedra intermedia, Ephedra equisetina Source: Healthnotes, Inc.; www.healthnotes.com

# Ephedra

Alternative names: Ephedra sinensis, Ma huang Source: Integrative Medicine Communications; www.drkoop.com

# Ephedra (Ma Huang)

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,777,00.html

# **Ephedra Sinensis**

Source: Integrative Medicine Communications; www.drkoop.com

# Eucalyptus

Alternative names: Eucalyptus globulus Source: Healthnotes, Inc.; www.healthnotes.com

# Eucalyptus

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,778,00.html

# **Evening Primrose**

Alternative names: Oenothera biennis, Sun Drop Source: Integrative Medicine Communications; www.drkoop.com

#### Feverfew

Alternative names: Tanacetum parthenium Source: Healthnotes, Inc.; www.healthnotes.com

# Feverfew

Alternative names: Tanacetum parthenium, Chrysanthemum parthenium Source: Integrative Medicine Communications; www.drkoop.com

#### Feverfew

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Feverfew

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

#### Feverfew

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com

Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,780,00.html

French Lavendar Source: Integrative Medicine Communications; www.drkoop.com

#### Gamma-linolenic Acid (GLA)

Source: Integrative Medicine Communications; www.drkoop.com

#### Ginger

Alternative names: Zingiber officinale Source: Healthnotes, Inc.; www.healthnotes.com

#### Ginger

Alternative names: Zingiber officinale Source: Integrative Medicine Communications; www.drkoop.com

#### Ginger

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Ginkgo

Alternative names: Ginkgo biloba Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

#### Ginkgo

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Ginkgo Biloba

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

#### Ginkgo Biloba

Source: Integrative Medicine Communications; www.drkoop.com

#### Ginkgo Biloba

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,788,00.html

#### Ginseng (Panax)

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10029,00.html

#### GLA

Source: Integrative Medicine Communications; www.drkoop.com

#### GLA (Gamma-linolenic Acid)

Source: Prima Communications, Inc.www.personalhealthzone.com

# **Glutamic Acid**

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

## Glutamine

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10030,00.html

# Glycyrrhiza Glabra

Source: Integrative Medicine Communications; www.drkoop.com

# Glycyrrhiza1

Alternative names: Licorice; Glycyrrhiza glabra L. Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

# Gotu Kola

Alternative names: Centella asiatica , Centella, March Pennywort, Indian Pennywort, Hydrocotyle, Brahmi (Sanskrit), Luei Gong Gen (Chinese)(Note: Gotu kola should not be confused with kola nut.) Source: Integrative Medicine Communications; www.drkoop.com

# Gotu Kola

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10031,00.html

# Green Tea

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

# Green Tea

Alternative names: Camellia sinensis Source: Integrative Medicine Communications; www.drkoop.com

# Green Tea

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10032,00.html

# Gugulipid

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10033,00.html

#### **Histamine H2 Antagonists**

Source: Integrative Medicine Communications; www.drkoop.com

#### Hong Qu

Source: Integrative Medicine Communications; www.drkoop.com

#### Hops

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

#### Horse Chestnut

Source: Prima Communications, Inc.www.personalhealthzone.com

## Horse Chestnut

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10037,00.html

#### Hung-chu

Source: Integrative Medicine Communications; www.drkoop.com

#### Huperzine a

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10038,00.html

#### Hydrocotyle

Source: Integrative Medicine Communications; www.drkoop.com

#### **Indian Pennywort**

Source: Integrative Medicine Communications; www.drkoop.com

# Indomethacin

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

#### Kava

Source: Prima Communications, Inc.www.personalhealthzone.com

# Kava Kava

Alternative names: Piper methysticum, Ava Source: Integrative Medicine Communications; www.drkoop.com

#### Ketorolac

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

#### Kudzu

Alternative names: Pueraria lobata Source: Healthnotes, Inc.; www.healthnotes.com

Lavandula Angustifolia Source: Integrative Medicine Communications; www.drkoop.com

# Lavender

Alternative names: Lavandula officinalis Source: Healthnotes, Inc.; www.healthnotes.com

# Lavender

Alternative names: Lavandula angustifolia, English Lavendar, French Lavendar Source: Integrative Medicine Communications; www.drkoop.com

# Lavender

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

# Licorice

Alternative names: Glycyrrhiza glabra, Spanish Licorice Source: Integrative Medicine Communications; www.drkoop.com

# Licorice

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,801,00.html

# Limetree

Source: Integrative Medicine Communications; www.drkoop.com

# Linden

Alternative names: Tilia cordata, Tilia platyphyllos, Limetree Source: Integrative Medicine Communications; www.drkoop.com

#### L-lysine

Source: Integrative Medicine Communications; www.drkoop.com

# Lysine

Alternative names: Amino Acid K, L-Lysine Source: Integrative Medicine Communications; www.drkoop.com

# Ma Huang

Source: Integrative Medicine Communications; www.drkoop.com

# Macrolides

Source: Integrative Medicine Communications; www.drkoop.com

# Mad-dog Skullcap

Source: Integrative Medicine Communications; www.drkoop.com

#### Maidenhair Tree

Source: Integrative Medicine Communications; www.drkoop.com

# Marsh Pennywort

Alternative names: Centella asiatica , Centella, March Pennywort, Indian Pennywort, Hydrocotyle, Brahmi (Sanskrit), Luei Gong Gen (Chinese)(Note: Gotu kola should not be confused with kola nut.) Source: Integrative Medicine Communications; www.drkoop.com

# Melaleuca

Alternative names: Tea Tree Oil; Melaleuca alternifolia Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org **Melatonin** Source: Healthnotes, Inc.; www.healthnotes.com

#### Melatonin

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,804,00.html

#### Mentha

Alternative names: Pennyroyal; Mentha/Hedeoma pulegium Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

#### Mentha X Piperita

Source: Integrative Medicine Communications; www.drkoop.com

# Methylsulfonylmethane

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

#### Metoclopramide

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

#### Minocycline Source: Healthnotes, Inc.; www.healthnotes.com

#### Mistletoe

Alternative names: Viscum album Source: Healthnotes, Inc.; www.healthnotes.com

#### **Mixed Amphetamines**

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

#### Monascus

Source: Integrative Medicine Communications; www.drkoop.com

# N-acetyl Cysteine

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

# N-acetyl Cysteine (nac)

Source: Prima Communications, Inc.www.personalhealthzone.com

# Nitroglycerin

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

#### Nitroglycerin

Alternative names: Deponit, Minitran, Nitrek, Nitro-Bid, Nitro-Derm, Nitro-Dur, Nitro-Time, Nitrocine, Nitrodisc, Nitrogard, Nitroglyn, Nitrol, Nitrolingual, Nitrong, NitroQuick, Nitrostat, Transderm-Nitro Source: Prima Communications, Inc.www.personalhealthzone.com

#### Non-steroidal Anti-inflammatory Drugs

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

# **Oenothera Biennis**

Source: Integrative Medicine Communications; www.drkoop.com

#### Panax

Alternative names: Ginseng; Panax ginseng Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

#### Panax Ginseng

Alternative names: Asian Ginseng Source: Integrative Medicine Communications; www.drkoop.com

#### Panax Quinquefolium

Alternative names: American Ginseng Source: Integrative Medicine Communications; www.drkoop.com

**Penicillin Derivatives** Source: Integrative Medicine Communications; www.drkoop.com

## Peppermint

Alternative names: Mentha piperita Source: Healthnotes, Inc.; www.healthnotes.com

#### Peppermint

Alternative names: Mentha x piperita Source: Integrative Medicine Communications; www.drkoop.com

#### Peppermint

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,812,00.html

#### Phenelzine

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

#### Phenylalanine

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

#### Phenylalanine

Source: Integrative Medicine Communications; www.drkoop.com

#### Phenylalanine

Source: Prima Communications, Inc.www.personalhealthzone.com

#### **Piper Methysticum**

Source: Integrative Medicine Communications; www.drkoop.com

#### Pollen

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

#### Progesterone

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

# Propranolol

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

#### Proton Pump Inhibitors (Gastric Acid Secretion Inhibitors)

Source: Integrative Medicine Communications; www.drkoop.com

#### Quinolones

Source: Integrative Medicine Communications; www.drkoop.com

#### Red Koji

Source: Integrative Medicine Communications; www.drkoop.com

#### **Red Leaven**

Source: Integrative Medicine Communications; www.drkoop.com

#### **Red Rice**

Source: Integrative Medicine Communications; www.drkoop.com

#### **Red Yeast Rice**

Alternative names: Angkak, Beni-koju, Hong Qu, Hung-chu, Monascus, Red Leaven, Red Rice, Red Koji, Zhitai, Xue Zhi Kang Source: Integrative Medicine Communications; www.drkoop.com

#### **Red Yeast Rice**

Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com Hyperlink: http://www.wholehealthmd.com/refshelf/substances\_view/0,1525,10054,00.html

#### Rosemary

Alternative names: Rosmarinus officinalis Source: Healthnotes, Inc.; www.healthnotes.com

#### Rosemary

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

#### **Royal Jelly**

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

#### Rue

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

#### S-Adenosylmethionine (SAMe)

Alternative names: SAMen Source: Integrative Medicine Communications; www.drkoop.com

#### Salsalate

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

#### SAMe

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

# SAMe

Alternative names: S-Adenosylmethionine (SAMe) Source: Integrative Medicine Communications; www.drkoop.com

#### Scutellaria Lateriflora

Source: Integrative Medicine Communications; www.drkoop.com

#### Sertraline

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

#### Skullcap

Alternative names: Scutellaria lateriflora, Mad-dog Skullcap Source: Integrative Medicine Communications; www.drkoop.com

#### **Spanish Licorice**

Source: Integrative Medicine Communications; www.drkoop.com

#### Sumatriptan

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

#### Sun Drop

Source: Integrative Medicine Communications; www.drkoop.com

#### Tanacetum

Alternative names: Feverfew; Tanacetum parthenium (L.) Schultz-Bip. Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

# **Tanacetum Parthenium**

Source: Integrative Medicine Communications; www.drkoop.com

#### Tanacetum V

Alternative names: Tansy; Tanacetum vulgare (L.) Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

**Tang Kuei** Source: Integrative Medicine Communications; www.drkoop.com

**Tetracycline Derivatives** Source: Integrative Medicine Communications; www.drkoop.com

#### **Thiazide Diuretics**

Source: Integrative Medicine Communications; www.drkoop.com

#### Thioridazine

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

#### Thymus

Alternative names: Thyme; Thymus vulgaris Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

#### Tilia Cordata

Source: Integrative Medicine Communications; www.drkoop.com

#### Tilia Platyphyllos

Source: Integrative Medicine Communications; www.drkoop.com

#### Timolol

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

#### Tyrosine

Source: Integrative Medicine Communications; www.drkoop.com

#### Uncaria Asian

Alternative names: Asian species; Uncaria sp. Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

#### **Uricosuric Agents**

Source: Integrative Medicine Communications; www.drkoop.com

#### Valerian

Alternative names: Valeriana officinalis Source: Integrative Medicine Communications; www.drkoop.com

#### Valeriana Officinalis

Source: Integrative Medicine Communications; www.drkoop.com

#### Vitex

Alternative names: Vitex agnus-castus Source: Healthnotes, Inc.; www.healthnotes.com

# White Willow

Source: Prima Communications, Inc.www.personalhealthzone.com

#### Willow

Alternative names: Salix alba Source: Healthnotes, Inc.; www.healthnotes.com

#### Willow Bark

Alternative names: There are several species of willow includingSalix alba, Salix nigra, Salix fragilis, Salix purpurea, Salix babylonica, White Willow, European Willow, Black Willow, Pussy Willow, Crack Willow, Purple Willow, Weeping Willow, Liu-zhi

Source: Integrative Medicine Communications; www.drkoop.com

#### Wood Betony

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

#### Zhitai

Source: Integrative Medicine Communications; www.drkoop.com

#### Zingiber

Alternative names: Ginger; Zingiber officinale Roscoe Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

# **Zingiber** Officinale

Source: Integrative Medicine Communications; www.drkoop.com

# Zolmitriptan

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

# Zue Zhi Kang

Source: Integrative Medicine Communications; www.drkoop.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 HEADACHE**

# Overview

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

# **Dissertations on Headache**

*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 headache. 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 Comparison of Psychotherapeutic Treatments for Muscle-contraction Headache by Drummond, Freddie Eugene, PhD from Texas A&M University, 1981, 123 pages http://wwwlib.umi.com/dissertations/fullcit/8128887
- A Randomized Controlled Trial of Internet-delivered, Self-help Treatment for Chronic Benign Headache: a Replication and Extension Study by Devineni, Trishul; PhD from State University of New York at Albany, 2002, 100 pages http://wwwlib.umi.com/dissertations/fullcit/3068765
- **Biofeedback Treatment Factors and the Alleviation of Migraine Headache** by Sellick, Scott Morgan; PhD from University of Alberta (Canada), 1982 http://wwwlib.umi.com/dissertations/fullcit/NK60383
- Cognitive-affective Factors in Chronic Headache by Demjen, Stefan; PhD from University of Calgary (Canada), 1986 http://wwwlib.umi.com/dissertations/fullcit/NL35941

- Cognitive-behavioral Treatment of Migraine Headache (stress Management, Biofeedback) by Berdine-Notarfonzo, Cathy, PhD from University of Toronto (canada), 1991, 214 pages http://wwwlib.umi.com/dissertations/fullcit/NN73773
- Control and Awareness of Digital Blood Volume Pulse a Comparison of Headache and Non-headache Subjects by Gainer John: PhD from McGill University (Canada)
- and Non-headache Subjects by Gainer, John; PhD from McGill University (Canada), 1986

http://wwwlib.umi.com/dissertations/fullcit/NL38255

- Coping in Children with Headache As Predictors of Adjustment and the Relationships between Parent and Child Coping Styles by Konyk, Debra L.; Ma from The University of Manitoba (Canada), 2002, 167 pages http://wwwlib.umi.com/dissertations/fullcit/MQ76982
- Coping Responses during Pain and Pain-free Periods in a Sample of Headache Sufferers by Lacroix, Renee; PhD from Queen's University at Kingston (Canada), 1989 http://wwwlib.umi.com/dissertations/fullcit/NL53443
- Electrophysiologic Evaluation and Treatment Effects in Patients with Tension-type Headache by Attia, Magdy Abdelmoiz; PhD from Texas Woman's University, 2002, 174 pages

http://wwwlib.umi.com/dissertations/fullcit/3059158

- Engendering Pain: Discourse on the Experience of Chronic Headache in the United States by Kryst, Sandra, PhD from University of Kentucky, 1995, 344 pages http://wwwlib.umi.com/dissertations/fullcit/9613666
- Evaluating the Role of Religious Coping in a Self-reported Headache Population by Buenaver, Luis Fernando; PhD from Virginia Commonwealth University, 2003, 161 pages

http://wwwlib.umi.com/dissertations/fullcit/3091824

- Headache and Depressed Affect in a Non-clinic College Student Population a Severity-continuum Analysis by Woods, Robert B; PhD from The University of Manitoba (Canada), 1988 http://wwwlib.umi.com/dissertations/fullcit/NL48042
- Home Versus Clinic-based Treatment for Pediatric Migraine Headache: Effects of Parental Involvement and Therapist Contact by Burke, Edmund Joseph, PhD from State University of New York at Albany, 1986, 273 pages http://wwwlib.umi.com/dissertations/fullcit/8614601
- Impact of a Minimal Provider Interaction Intervention on Headache Selfmanagement: a Self-efficacy Approach by Bond, Dale Scott; PhD from The University of Utah, 2002, 255 pages
  http://www.lib.umi.com/discontations/fulleit/2042420

http://wwwlib.umi.com/dissertations/fullcit/3043429

- Issues in the Rehabilitation of Persons with Post-traumatic Headache: a Long-term Follow-up Descriptive Study (headache) by Snavely, Clarella Marie Guider, PhD from The University of Iowa, 1992, 263 pages http://wwwlib.umi.com/dissertations/fullcit/9237012
- Migraine Headaches: Coping Efficacy of Guided Imagery Therapy by Ilacqua, Giorgio, EDD from University of Toronto (Canada), 1991, 155 pages http://wwwlib.umi.com/dissertations/fullcit/NN78744

- Nonpharmacological Treatment of Menstrual Headache: Relaxation-biofeedback Behavior Therapy and Person-centered Insight Therapy (rogerian) by Szekely, Barbara Caroline, PhD from University of Pittsburgh, 1984, 152 pages http://wwwlib.umi.com/dissertations/fullcit/8514985
- Post Dural Puncture Headache Following Continuous Spinal Anesthesia in the Morbidly Obese Parturient by Coker, Lanny Leon; DNSC from The University of Tennessee Center for the Health Sciences, 2002, 31 pages http://wwwlib.umi.com/dissertations/fullcit/3067788
- Post-traumatic Headache: Psychological Sequelae and Treatment Outcome by Tatrow, Kristin Jennifer; PhD from State University of New York at Albany, 2002, 146 pages http://wwwlib.umi.com/dissertations/fullcit/3063958
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# **Keeping Current**

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# **CHAPTER 5. CLINICAL TRIALS AND HEADACHE**

# Overview

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

# **Recent Trials on Headache**

The following is a list of recent trials dedicated to headache.<sup>8</sup> Further information on a trial is available at the Web site indicated.

#### • Psychological Assessment and Treatment of Chronic Benign Headache

Condition(s): Headache; Migraine; Tension Headache; Stress Headache; Vascular Headache

Study Status: This study is currently recruiting patients.

Sponsor(s): Department of Veterans Affairs Medical Research Service

Purpose - Excerpt: Subjects with chronic migraine or tension headaches will receive 12 sessions of biofeedback or relaxation training after fulfilling screening, intake interviews, & psychological testing requirements. They will chart headache pain, anger level, & medication usage throughout baseline, treatment, and 3 month follow-up periods. Migraine sufferers will receive a combination of progressive muscle relaxation training and thermal biofeedback (learning to warm hands). Subjects are randomly assigned to receive treatment either in the office with the therapist or from another room (where communication will be over a computer). The research is designed to compare the effectiveness of treatment based on location. Tension headache sufferers will receive training in how to reduce their muscle tension levels. They will be randomly assigned to have equipment monitor muscle tension levels either in the forehead or shoulder regions. The research is designed to compare the effectiveness of feedback to the forehead versus the shoulder muscles.

Study Type: Interventional

Contact(s): see Web site below

<sup>&</sup>lt;sup>8</sup> These are listed at **www.ClinicalTrials.gov**.

Web Site: http://clinicaltrials.gov/ct/show/NCT00018811

• A Phase III Study of Civamide Nasal Solution (Zucapsaicin) for the Treatment of Episodic Cluster Headache

Condition(s): Episodic Cluster Headache

Study Status: This study is no longer recruiting patients.

Sponsor(s): Winston Laboratories

Purpose - Excerpt: This is a 49-day study to evaluate the effectiveness of Intranasal Civamide (Zucapsaicin) in the treatment of an episodic cluster headache period compared to placebo (medically inactive substance which does not contain any active ingredients).

Phase(s): Phase III

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00033839

# • Intranasal Civamide for Episodic Cluster Headache

Condition(s): Episodic Cluster Headache

Study Status: This study is no longer recruiting patients.

Sponsor(s): Winston Laboratories

Purpose - Excerpt: This is a 49-day study to evaluate the effectiveness of Intranasal Civamide (Zucapsaicin) in the treatment of an episodic cluster headache period compared to placebo (medically inactive substance which does not contain any active ingredients).

Phase(s): Phase III

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00069082

# • A Study to Measure the Safety and Effectiveness of Zonisamide in Subjects with Migraine Headache

Condition(s): Migraine Headache

Study Status: This study is completed.

Sponsor(s): Elan Pharmaceuticals

Purpose - Excerpt: The purpose of this study is to determine if zonisamide is effective as a preventative medication for individuals with migraine headache.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00055484

# Women's Use of Alternative Medicine: A Multiethnic Study

Condition(s): Uterine Fibroids; Osteoporosis; Urinary Tract Infection; High Blood Pressure; Heart Disease; Arthritis; Depression; Headaches

Study Status: This study is completed.

Sponsor(s): National Center for Complementary and Alternative Medicine (NCCAM)

Purpose - Excerpt: The purpose of this study is to examine socio-cultural factors of women's use of complementary and alternative medicine (CAM). The effects of socioeconomic status, social networks and acculturation on CAM use will be assessed among white, African-, Mexican-, and Chinese-American women.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00067249

# **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 "headache" (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. PATENTS ON HEADACHE**

# Overview

Patents can be physical innovations (e.g. chemicals, pharmaceuticals, medical equipment) or processes (e.g. treatments or diagnostic procedures). The United States Patent and Trademark Office defines a patent as a grant of a property right to the inventor, issued by the Patent and Trademark Office.<sup>9</sup> Patents, therefore, are intellectual property. For the United States, the term of a new patent is 20 years from the date when the patent application was filed. If the inventor wishes to receive economic benefits, it is likely that the invention will become commercially available within 20 years of the initial filing. It is important to understand, therefore, that an inventor's patent does not indicate that a product or service is or will be commercially available. The patent implies only that the inventor has "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States. While this relates to U.S. patents, similar rules govern foreign patents.

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

# Patents on Headache

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

<sup>&</sup>lt;sup>9</sup>Adapted from the United States Patent and Trademark Office:

http://www.uspto.gov/web/offices/pac/doc/general/whatis.htm.

will tell you how to obtain this information later in the chapter. The following is an example of the type of information that you can expect to obtain from a patent search on headache:

# • Acupressure pillow apparatus and method

Inventor(s): Myler; Scott G. (354 E. Heather Rd., Orem, UT 84057)

Assignee(s): none reported

Patent Number: 6,305,040

Date filed: June 3, 1999

Abstract: An Acupressure pillow provides selective pressure by location and force applied to a body of a user. By selection of a body member, a location on that body member, and a pressure point thereat, an acupressure pillow may be used for gauging and applying a localized, selective force or pressure at a designated point for a user. For example, **headaches** have been attributed to various causes including stress, tension, and so forth, all of which may result in involuntary tightening of muscles. Tightening of muscles affects blood flow. Restriction of blood flow may be responsible for certain **headache** pain. By applying a steady, predictable, reliable, continuing pressure at a designated acupressure location on member of a body of a user, muscles may be relaxed. Massage therapy requires knowledgeable application of pressure and motion. An acupressure pillow applies steady pressure, to which the body will become accustomed and relax. The actual continual application of pressure may tend to speed relaxation better than unpredictable motion such as vibration and other techniques used in the art.

Excerpt(s): This invention relates to physical therapy and, more particularly, to novel systems and methods for selectively applying pressure to designated locations on a member of a human body in order to provide relaxation of muscles for therapeutic effect. Massage therapy has been known for several years, even decades or more. Within the established medical community within the United States and other countries of the world, massage therapy has gained increased recognition for the therapeutic benefits available by selective application of regular motion and pressure to muscles of the body in order to relieve tension and provide associated benefits. Chiropractic medicine has gained favor as persons treated thereby become satisfied that they feel better. Regardless of the school that one subscribes to, feeling healthy is one ultimate measure of success of any treatment. In Asian countries, ancient arts have been practiced that have only recently become known, acknowledged, applied, investigated, and the like, within the Western Hemisphere. For example, acupuncture involves the use of carefully placed and manipulated needles for providing relief of various symptoms.

Web site: http://www.delphion.com/details?pn=US06305040\_\_\_

# • Apparatus for administering composition for inhibiting cerebral neurovascular disorders and muscular headaches

Inventor(s): Levin; Bruce H. (241 S. 6th St., Philadelphia, PA 19106)

Assignee(s): none reported

Patent Number: 6,491,940

Date filed: January 27, 2000

Abstract: Methods, kits, apparatus, and compositions for inhibiting a cerebral neurovascular disorder or a muscular **headache** in a human patient are provided. The methods comprise intranasally administering to the patient a pharmaceutical composition comprising a local anesthetic, and preferably a long-acting local anesthetic ingredient. A composition useful for practicing the methods of the invention is described which comprises at least one local anesthetic in a pharmaceutically acceptable carrier, wherein the composition is formulated for intranasal delivery. Cerebral neurovascular disorders include migraine and cluster **headache**. Muscular **headaches** include tension **headaches** and muscle contraction **headaches**. A kit comprising the composition and an intranasal applicator and a method of systemically delivering a pharmaceutically active agent to an animal are also included in the invention. Apparatus for delivering or applying the compositions of the invention or for performing the methods of the invention are also described.

Excerpt(s): This invention relates to compositions, kits, methods, and apparatus for inhibiting muscular **headaches** and cerebral neurovascular disorders including, but not limited to, neurovascular **headaches**, migraines, cluster **headaches**, tinnitus, cerebrovascular spasm, ischemic disorders, and seizures. Headache is a common symptom of numerous diseases and disorders including, but not limited to, migraine, muscle tension, systemic or intracranial infection, intracranial tumor, head injuries, severe hypertension, cerebral hypoxia, certain diseases of the eyes, nose, throat, teeth, and ears, and **head pain** for which no cause can be determined. Infrequent **headaches** can often be determined to result from causes attributable to a particular experience of a patient, such as fatigue, fever, alcohol ingestion, muscle contraction, tension, or the like. The cause of persistent or recurrent **headaches** is often difficult to determine. Persistent or recurrent **headaches** include, but are not limited to, muscular **headaches**, such as tension or muscle contraction **headaches**, and neurovascular **headaches**, such as migraines and cluster **headaches**.

Web site: http://www.delphion.com/details?pn=US06491940\_\_\_

#### • Composition for treating migraine headaches

Inventor(s): Hendrix; Curt (17401 Ventura Blvd., Encino, CA 92705)

Assignee(s): none reported

Patent Number: 6,500,450

Date filed: April 27, 2000

Abstract: The present invention relates to a dietary supplement for the treatment of migraine **headache**. An extract of the feverfew plant containing parthenolide in combination with magnesium, with or without riboflavin, provided significant reduction of migraine **headaches** and the associated symptoms. The magnesium is present as a combination of magnesium oxide and a magnesium salt of an organic acid. The ratio of magnesium to parthenolide was about 450:1

Excerpt(s): The present invention provides a dietary supplement which supplies a combination of prophylactic and restorative components which assist the body in maintaining normal cerebrovascular tone and reduces the symptoms of migraine **headaches**. Migraine has been a well-known medical problem for over 5,000 years and represents one of the most investigated types of **head pain**. Epidemiological research has shown that in the United States, 18% of women and 6% of men suffer from migraine **headaches**. This extrapolates to approximately 18 million females and 5.6 million males

over the age of 12 with this disorder. The prevalence of migraine, according to the Center for Disease Control, has increased 60% from 1981 to 1989. While migraine can occur at any age, 30% of migraine sufferers report their first attack before the age of ten, and the condition is most common in adolescents and young adults. The economic impact of migraine is staggering, with annual cost of the disease estimated at 18 billion dollars. consistent biochemical or physiological characteristic has yet to be identified in the relatives of those afflicted with the conditions.

Web site: http://www.delphion.com/details?pn=US06500450\_\_\_

# • Compositions and methods for relieving headache symptoms in aspirin-sensitive headache sufferers

Inventor(s): Frank-Kollman; Mary Theresa (173 Egrets Way, Richmond Hill, GA 31324)

Assignee(s): none reported

Patent Number: 6,440,983

Date filed: December 21, 2000

Abstract: The treatment of migraine and/or cluster **headaches** in human beings in need of such treatment includes oral administration of a composition containing acetaminophen, ibuprofen, caffeine and magnesium as the active ingredients. The inclusion of an additional active ingredient, guaifenesin, further provides treatment for severe sinus **headaches**. Compositions and methods for alleviating the symptoms of these **headache** conditions are disclosed.

Excerpt(s): The present invention relates broadly to the field of healthcare, and in particular, to the treatment of severe headaches in human beings. More specifically, this invention relates to compositions and methods for providing relief from the symptoms of migraine headaches and/or cluster headaches and/or headaches related to sinus congestion, in affected individuals who also have a low tolerance for aspirin due to digestive disorders. Migraine is a particularly painful headache, which recurs and can be physically debilitating to sufferers. In many respects, cluster headaches are similar to migraine **headaches**, and all references herein to migraine and/or migraine **headaches** shall be considered as also including, and as references to, cluster headaches. There is no single cause or remedy for migraine headaches, and the incidence of migraine appears to be increasing in the general population. Although sufferers, on average, experience only one attack per month, each attack can last between four and seventytwo hours. In some cases, sufferers experience a pre-onset "warning" which may indicate that a migraine is imminent, and which may be termed an "aura." An "aura" is a disruption of brain function characterized by visual disturbances like flashing lights and blurred vision. These "disruptions" occur twenty to thirty minutes before an attack. About twenty percent of migraine suffers experience "aura" symptoms. Other attacks can be preceded by a "prodrome" several hours before the onset of a migraine. These "prodrome" symptoms may include, but are not limited to, fatigue, yawning, sensory sensitivity, mood changes, and food cravings. Prescription medications have previously been developed to alleviate the severity of migraine pain, but prescription migraine medications generally contain some type of narcotic, which, over time, may become addictive. Although over-the-counter remedies also exist, marketed under the EXCEDRIN.RTM. and ADVIL.RTM. brands, the EXCEDRIN.RTM. Migraine Formula contains aspirin, acetaminophen, and caffeine as its active ingredients, while the only active ingredient of the ADVIL.RTM. Migraine product is ibuprofen. Many migraine sufferers cannot take aspirin, due to digestive disorders, such as acid reflux disease,

ulcers, and acid indigestion, and for many such sufferers, ibuprofen alone is not sufficient to lessen the pain or to reduce it to a manageable level. It would therefore be desirable to provide a non-prescription remedy which alleviates migraine symptoms in a manner not accomplished by the currently available "over-the-counter" remedies.

Web site: http://www.delphion.com/details?pn=US06440983\_\_\_

# • Compositions for treating allergic and other disorders using norastemizole in combination with other active ingredients

Inventor(s): Aberg; A. K. Gunnar (Westborough, MA), Woosley; Raymond L. (Washington, DC)

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

Patent Number: 6,303,632

Date filed: April 16, 2001

Abstract: Methods and compositions are disclosed utilizing metabolic derivatives of astemizole for the treatment of allergic disorders while avoiding the concomitant liability of adverse effects associated with the astemizole. The metabolic derivatives of astemizole are also useful for the treatment of retinopathy and other small vessel disorders associated with diabetes mellitus and such other conditions as may be related to the antihistamine activity of astemizole. For example, the metabolic derivatives of astemizole are useful for the treatment of asthma, motion sickness, and vertigo, without the concomitant liability of adverse effects associated with astemizole. Furthermore, the metabolic derivatives of astemizole, in combination with non-steroidal anti-inflammatory agents or other non-narcotic analgesics, or in combination with a decongestant, cough suppressant/antitussive or expectorant, are useful for the treatment of cough, cold, cold-like, and/or flu symptoms and the discomfort, headache, pain, fever, and general malaise associated therewith, without the concomitant liability of adverse effects associated therewith without the concomitant liability of adverse effects associated therewith astemizole.

Excerpt(s): This invention relates to novel pharmaceutical compositions containing desmethylastemizole, 6-hydroxydesmethylastemizole and norastemizole. These compositions possess potent antihistaminic activity and are useful in treating allergic rhinitis, asthma and other allergic disorders while avoiding adverse effects associated is with the administration of other antihistamines, such as astemizole, including but not limited to cardiac arrhythmias, drowsiness, nausea, fatigue, weakness and headache. Also, these compositions, in combination with non-steroidal anti-inflammatory agents or other non-narcotic analgesics, are useful for the treatment of cough, colds cold-like, and/or flu symptoms and the discomfort, headache, pain, fever, and general malaise associated therewith. The aforementioned combinations may optionally include one or other including decongestant, more active components а cough suppressant/antitussive, or expectorant. Additionally, these novel pharmaceutical compositions containing desmethylastemizole, 6-hydroxydesmethylastemizole and norastemizole are useful in treating motion sickness, vertigo, diabetic retinopathy, small vessel complications due to diabetes and such other conditions as may be related to the activity of these derivatives as antagonists of the H-1 histamine receptor while avoiding the adverse effects associated with the administration of other antihistamines, such as astemizole. Also disclosed are methods for treating the above-described conditions in a human while avoiding the adverse effects that are associated with the administration of other antihistamines, such as astemizole, by administering the aforementioned

pharmaceutical compositions containing desmethylastemizole, 6hydroxydesmethylastemizole and norastemizole to said human.

Web site: http://www.delphion.com/details?pn=US06303632\_\_\_

# • Compositon containing medicinal herbs and young antlers of cornu cervi

Inventor(s): Han; Wan-Seok (#610-4, Shinsa-dong, Kangnam-ku, 135-894, Seoul, KR)

Assignee(s): none reported

Patent Number: 6,444,236

Date filed: August 27, 2001

Abstract: A composition is provided for use in health foods for promoting the circulation of blood, prepared from medicinal herbs, including Lycium chinense Miller, Agastache rugosa (Fischer et Meyer) O. Kuntze, Pueraria lobat Ohwi, Macrocarpium officinale Sieb. et Zucc., Gastrodia elata blume, Amomum xanthioides Wallich, Cratagegus pinnatifida Bge., Aquillaria Agallocha Roxburgh, Inula Helenium L., Cassia obtusifolia L., and Rubus sachalinensis Lev., and young antlers of Cornu cervi. In addition to being safe to the body, the composition exhibits excellent pharmaceutical effects of treating arteriosclerosis and alleviating the **headache** attributed to the disturbance of blood circulation.

Excerpt(s): The present invention relates, in general, to a composition of health foods for promoting the circulation of blood and, more particularly, to a composition made of medicinal herbs, Lycium chinense Miller, Agastache rugosa (Fischer et Meyer) O. Kuntze, Pueraria lobat Ohwi, Macrocarpium officinale Sieb. et Zucc., Gastrodia elata blume, Amomum xanthioides Wallich, Cratagegus pinnatifida Bge., Aquillaria Agallocha Roxburgh, Inula Helenium L., Cassia obtusifolia L., and Rubus sachalinensis Lev., and young antlers of Cornu cervi, suitable for use in health foods helpful in improving blood circulation. At present, various electrical and electronic instruments are generally used in offices for office automation and even in home for home automation. On the whole, such instruments require the user to assume certain postures, for example, to maintain his or her arms at a distance from the body, for their operation. Accordingly, after operating the instruments for a long time of period, the user is liable to undergo stiffness at certain body sites, such as arms, legs, waist, etc. In most cases, stiffened muscles can be easily relieved simply by massaging them. However, once afflicted with muscular stiffness, those who operate such instruments every day have difficulty in healing the discomfort or pain. In addition to the operation of OA instruments, exercise, physical work, inappropriate posture, and metal stress are found to cause muscular stiffness. Other causes of muscular stiffness are exemplified by cervical spondylosis, thoracic outlet syndrome, hypertension, asthenopia, autonomous dysmyotonia, and menoposal disorder. Symptoms of the stiffness include characteristic chronic pain, irritability, and, in severe cases, headache and emesis.

Web site: http://www.delphion.com/details?pn=US06444236\_\_\_

#### • Formulations and methods for treating chronic migraine

Inventor(s): Marrongelle; Jeffrey L. (1629 Long Run Rd., Orwigsburg, PA 17972), Staverosky; Thomas J. (1537 Mineral Springs Rd., Reading, PA 19602)

Assignee(s): none reported

Patent Number: 6,517,832

Date filed: August 24, 2001

Abstract: A prophylactic treatment for the human malady clinically described as migraine **headache** comprising daily administration in unit dosage form of a first formulation which comprises a major amount of bioactive peptides and a minor amount of probiotics. Concurrently, daily administration in dosage form of a second formulation of a major amount of active components like malic acid, sylibum marianum, acetyl-L-cysteine, copper chelate, zinc gluconate, aspartate and bromelain. A minor amount of plant derivatives excipients comprise the balance of the second formulation. Preferably, these plant derivatives include beet root, powder, watercress, celery, dandelion, capsicum and artichoke extract.

Excerpt(s): This is a non-provisional patent specification and claims submitted for an official filing receipt under Patent Code 111(a). Headaches range from the rare and excruciating type, known as clusters, through the common tension-type (stressinduced), to the somewhat less common, but notorious, migraine, with or without an aura effect. Migraines have been attributed to blood vessels in the brain being constricted and then relaxing, thus altering blood flow. It was thought early on that the pain of migraine was of vascular origin and caused by excessive dilation of branches of the common carotid artery bed. Currently, researchers are zeroing in on the trigeminal nerve system, and the nerve chemical Serotonin, in particular, as one set of candidate headache pain culprits. While significant advances have been made in dealing with the pain of migraine, little has had a dramatic effect in preventing the next attack or curing the disease. Indeed, the dominant medical community generally describes migraine as an incurable disease of unknown cause. Many migraine sufferers have reached a level of total frustration due to the lack of help they receive from the dominate or alternative medical community. Most have visited multiple health care professionals and have tried numerous prescription, over the ouncter, and natural products in an attempt to find a solution.

Web site: http://www.delphion.com/details?pn=US06517832\_\_\_

#### • Headache treatment and method

Inventor(s): Devi-Jonnalagadda; Venkata Thirumala (104 Peachtree Dr., Jacksonville, NC 28546), Jonnalagadda; Murali M. R. (104 Peachtree Dr., Jacksonville, NC 28546)

Assignee(s): none reported

Patent Number: 6,350,465

Date filed: January 17, 2001

Abstract: A method of treating **headaches** by blocking the sphenopalatine ganglion comprises using a first device to anesthetize a front portion of the nasal cavity. A second device is used to anesthetize a rear portion of the nasal cavity. After these priming anesthetizations, a primary pain medication delivery device is used to discharge an anesthetic to the sphenopalatine ganglion to treat the **headache**.

Excerpt(s): The present invention relates to a set of devices and a technique for treating headaches and particularly migraines. Severe headaches are suffered by large numbers of the American population. It is estimated that 1 in 10 males and 1 in 4 females experience debilitating headaches regularly. Even larger percentages may experience the occasional mild headache capable of being treated with an over the counter analgesic, such as aspirin, ibuprofen, or acetaminophen. Severe headaches may substantially incapacitate the individual suffering from the headache. Such incapacitation may lead to losses in productivity, inability to work, and a general deterioration of quality of life. There are presently two techniques by which severe headaches are treated with a sphenopalatine ganglion block. Both of these techniques involve treatment by a medical provider in an office or hospital setting. The first technique comprises using a rigid cotton swab coated with a pain medication. The cotton swab is inserted through the nasal passage to the sphenopalatine ganglion. The cotton tip then swabs the area near the ganglion to introduce the pain medication thereto. The rigid swab may cause trauma to the nasal cavity and cause other discomfort to the individual enduring the treatment.

Web site: http://www.delphion.com/details?pn=US06350465\_\_\_

• Intraoral topical anti-inflammatory treatment for relief of migraine, tension-type headache, post-traumatic headache, facial pain, and cervical-muscle spasm

Inventor(s): Friedman; Mark (5 Forest Ct., Larchmont, NY 10538)

Assignee(s): none reported

Patent Number: 6,423,697

Date filed: July 26, 2000

Abstract: An anti-inflammatory, either a NSAID or glucocorticoid steroid in the form of an ointment, cream, lotion, gel, powder, tablet, paste, film, tape or adhesive bandage, provided with appropriate vehicle to allow specific adherence to specific gingival areas, for topical treatment of inflammation. This composition and the method of using same is used to prevent or relieve migraine, tension-type **headache**, post-traumatic **headache**, facial pain and cervical muscle spasm.

Excerpt(s): This invention relates to a method for treatment of migraine, tension-type headache, post-traumatic headache, facial pain and cervical-muscle spasm. More particularly the invention relates to a method of treatment which is non-invasive, nontoxic and non-sedating. The method of the invention comprises delivering a composition, topically, to a specific intraoral area of tenderness consistently noted in patients with **headache** that appears closely associated with several painful conditions: migraine, tension-type headache, post-traumatic headache, facial pain and cervicalmuscle spasm. The composition comprises at least one member of the group of antiinflammatory agents, NSAIDS or glucocorticoid steroids dissolved, distributed or dispersed in a suitable carrier for topical administration to the intraoral area of tenderness which has been found to be associated with the afore-noted conditions. In preliminary data analysis, 1026/1100 (93.2%) mostly asymptomatic migraine patients exhibited maxillary alveolar tenderness, with laterality and degree of tenderness closely related to laterality and severity of symptoms. This consistent finding has been corroborated by several neurologists. In a pilot study of thirty asymptomatic migraine patients with a unilateral history, blinded, inexperienced examiners selected the symptomatic side in 27/30 (90%) patients, based on the laterality of intraoral palpation findings.

Web site: http://www.delphion.com/details?pn=US06423697\_\_\_

#### Means and method for the treatment of migraine headaches

Inventor(s): Fischell; David R. (Fair Haven, NJ), Fischell; Robert E. (Dayton, MD), Upton; Adrian R. M. (Dundas, CA)

Assignee(s): NeuraLieve, Inc. (Glenelg, MD)

Patent Number: 6,402,678

Date filed: July 31, 2000

Abstract: Disclosed is a means and method for the treatment of migraine **headaches**. Patients who have migraine **headaches** typically have a band of excited brain neurons that are a precursor of the **headache**. By placing an intense alternating magnetic field onto a certain region of the brain, an electrical current can be generated in the cerebral cortex that can depolarize these excited brain neurons. This procedure can stop a migraine **headache** in some patients or at least decrease its severity. The device to perform this function can be called a "magnetic depolarizer". The magnetic depolarizer can be placed in some headgear such as a bicycle helmet in order to place the magnetic field at the correct location relative to the patient's cerebral cortex. This technique can be particularly valuable for patients who have a perceptible aura that occurs prior to the onset of a migraine **headache**. A visual aura caused by the progression of an excited band of neurons in a patient's occipital lobe, which aura occurs 20 to 30 minutes prior to the onset of **head pain**, would be particularly well treated by means of the magnetic depolarizer.

Excerpt(s): Migraine headaches occur in approximately 12% of the world population. Therefore, in the United States in the year 2000 there are approximately 30 million people who suffer from this affliction. Although medicines have been created that significantly diminish the suffering of migraine patients, the medicines often have highly undesirable side effects and many patients do not obtain satisfactory relief from the severe **headache** pain and other discomforts associated with migraine. Furthermore, migraine headaches are typically treated after they have become painful, i.e., the treatment is often ineffective in preventing the onset of the migraine headache. Other than some drugs for some patients, there is no known treatment for migraine headaches that can be applied after a patient detects an aura of that **headache** to prevent the occurrence of pain and other undesirable manifestations of that migraine headache. A non-invasive, non-drug method for preventing the occurrence of migraine headaches would be a remarkable boon for those millions of people all over the world who suffer from these painful experiences. In 1985, A. T. Barker, et al (Lancet, 1985, pp. 1105-1107) described the use of a coil placed over the scalp which produced a high intensity, time varying, magnetic field. This magnetic field produces an electric current in the cortex of the human brain which can in turn produce certain effects on brain neurons. By the year 2000, this type of system was given the name Transcranial Magnetic Stimulation (TMS). If repetitive magnetic pulses are applied in this manner, it has been given the name rTMS. In the journal Neurology (Apr. 11, 2000, pp. 1529-1531) it has been reported by B. Boroojerdi, et al that rTMS at a rate of one pulse per second can create a reduction of the excitability of the neurons of the human visual cortex. However, no prior art has indicated that rTMS can be used for the preventing the occurrence of migraine headaches.

Web site: http://www.delphion.com/details?pn=US06402678\_\_\_\_

# • Method for treating headache

Inventor(s): Aoki; K. Roger (Laguna Hill, CA), Carlson; Steven R. (Laguna Niguel, CA), Grayston; Michael W. (Irvine, CA), Leon; Judith M. (Laguna Niguel, CA)

Assignee(s): Allergan, Inc. (Irvine, CA)

Patent Number: 6,458,365

Date filed: January 19, 2000

Abstract: A method and composition for treating a patient suffering from a disease, disorder or condition and associated pain include the administration to the patient of a therapeutically effective amount of a neurotoxin selected from a group consisting of Botulinum toxin types A, B, C, D, E, F and G.

Excerpt(s): The present invention provides novel methods for treating various disorders and conditions, with Botulinum toxins. Importantly, the present invention provides methods useful in relieving pain related to muscle activity or contracture and therefore is of advantage in the treatment of, for example, muscle spasm such as Temporomandibular Joint Disease, low back pain, myofascial pain, pain related to spasticity and dystonia, as well as sports injuries, and pain related to contractures in arthritis. Heretofore, Botulinum toxins, in particular Botulinum toxin type A, has been used in the treatment of a number of neuromuscular disorders and conditions involving muscular spasm; for example, strabismus, blepharospasm, spasmodic torticollis (cervical dystonia), oromandibular dystonia and spasmodic dysphonia (laryngeal dystonia). The toxin binds rapidly and strongly to presynaptic cholinergic nerve terminals and inhibits the exocytosis of acetylcholine by decreasing the frequency of acetylcholine release. This results in local paralysis and hence relaxation of the muscle afflicted by spasm. For one example of treating neuromuscular disorders, see U.S. Pat. No. 5,053,005 to Borodic, which suggests treating curvature of the juvenile spine, i.e., scoliosis, with an acetylcholine release inhibitor, preferably Botulinum toxin A.

Web site: http://www.delphion.com/details?pn=US06458365\_\_\_

# Pressure application apparatus for reducing stress and relieving headaches

Inventor(s): Guest; Jack (1120 Oro Vista, Litchfield Park, AZ 85340)

Assignee(s): Guest; Jack ()

Patent Number: 6,315,743

Date filed: June 23, 1998

Abstract: An apparatus for applying substantially constant pressures to the temple areas of a user's head, thereby relieving the user's **headache** is provided. A preferred embodiment of the apparatus comprises a C-shaped frame member which fits over the top of the user's head such that each end of the frame member is substantially aligned with a respective one of the user's two temple areas. Each end of the frame member is further coupled to a head contact assembly which, in use, is pressed against a respective one of the two temple areas of the user's forehead. Each head contact assembly is useradjustable, preferably comprising a threaded screw member which screws through a corresponding threaded hole in a respective end of the C-shaped frame member. This allows the user to turn the head contact assembly either clock-wise or counter clockwise, effectively increasing or decreasing the amount of pressure applied by the apparatus to each of the user's respective temple areas. The apparatus may also include a height adjustment assembly coupled to the top of the C-shaped frame member which allows the user to adjust the height of the frame member above his or her head, thereby adjusting the vertical position of the two head contact assemblies with respect to the user's respective temple areas.

Excerpt(s): It is known that applying pressure to a person's forehead and/or scalp tends to help to dramatically reduce stress and relieve **headaches**. Typically, a person will do so by pressing and/or rubbing his or her fingers against the particular areas on the head that result in the greatest comfort. Often the pressure is applied through massage, and to this end, a number of inventions have been derived in attempt to replicate the use of one's hands by providing massage apparatuses which fit around a user's head. For examples of various head-massaging apparatuses, see Carlson, U.S. Pat. No. 2,482,838, issued Nov. 4, 1947; La Verne, U.S. Pat. No. 2,664,884, issued Jan. 5, 1954; and Chester, U.S. Pat. No. 4,506,659, issued Mar. 26, 1985. However, the above-mentioned apparatuses are typically complicated, heavy, expensive to manufacture, uncomfortable to use, and/or inherently aesthetically displeasing for use in public or work environments. Furthermore, these apparatuses have generally failed to recognize that the application of a static and constant pressure to the temple areas of one's forehead can provide equal or even greater success in relieving stress and headaches than the above-mentioned massaging techniques. Accordingly, an invention is needed which recognizes the benefits of applying a constant and static pressure to the temple areas and further provides a light-weight, inexpensive, comfortable, and inherently aesthetically pleasing apparatus which can be worn at home, work, or in public. In accordance with one preferred embodiment of the present invention, a C-shaped rigid frame member may be provided which substantially fits over the top of a user's head. Each end of the frame member suitably includes a threaded hole for accepting a screwlike head contact assembly. Moreover, a third threaded hole may be provided at the top of the C-shaped frame member for accepting a height adjustment assembly.

Web site: http://www.delphion.com/details?pn=US06315743\_\_\_

#### • Pressure application device and method for ameliorating migraine headache

Inventor(s): Schroer; Frederikus Johannes (Laurierstraat 89 hs. 1016PJ, Amsterdam, Holland, NL)

Assignee(s): none reported

Patent Number: 6,638,295

Date filed: March 22, 2000

Abstract: Disclosed is an apparatus and method for aiding in compressing an extracranial blood vessel, the apparatus having a biasing member, or spring, for producing a constant force, and two elongated curved arms connected to the biasing member for transmitting the force. The connected arms define a substantially elliptical curve having the biasing member positioned along a major axis of the elliptical curve, and a pressure applicator connected to each arm for applying the force to the skin in the form of pressure, to thereby aid in compressing the underlying blood vessel. Each arm comprises a proximal arm portion connected to the spring, a distal arm portion pivotably connected to the proximal arm portion, and a pressure applicator connected to the distal arm portion. The device is substantially foldable by pivoting each distal arm portion to a position alongside its proximal arm portion, thereby folding the arm. The pressure may be applied with motion to thereby provide a substantially massaging action.

Excerpt(s): The present invention relates to the field of **headaches** and, more particularly, to a pressure application device for aiding in compressing an extracranial blood vessel underlying the skin of the head, the device helping to substantially ameliorate a classic migraine **headache**. Migraine is a periodically recurring **headache** which generally manifests as a very localized **headache**. It is estimated that approximately 10% of the population suffers from a more or less serious form of migraine **headache**. There are numerous forms of migraine, but generally a classic migraine attack consists of two important, distinct phases. There is a first pre-headache phase, also known by some as the aura stage. The pre-headache stage is often without pain, but with specific pre-headache symptoms. These symptoms may include, for example, visual disturbances including images of colored bubbles, lines and the like, or other disturbances of the various senses, for example in hearing or the senses of taste and smell. Often, a spot of light known as the "aura", is seen by the migraine patient during this pre-headache phase. Numbness or tingling of parts of the body, such as fingers, hands, lips and the like, has also been reported to occur.

Web site: http://www.delphion.com/details?pn=US06638295\_\_\_

# • Substituted azole derivatives as inhibitors of corticotropin releasing factor

Inventor(s): Dubowchik; Gene M. (Middlefield, CT), Zuev; Dmitry S. (Wallingford, CT)

Assignee(s): Bristol-Myers Squibb Company (Princeton, NJ)

Patent Number: 6,515,005

Date filed: September 17, 2001

Abstract: The present invention relates to thiazoles, oxazoles, imidazoles and pharmaceutical compositions comprising said compounds antagonizing the corticotropin releasing factor receptor ("CRF receptor") and useful for the treatment of depression, anxiety, affective disorders, feeding disorders, post-traumatic stress disorder, **headache**, drug addiction, inflammatory disorders, drug or alcohol withdrawal symptoms and other conditions the treatment of which can be effected by the antagonism of the CRF-1 receptor.

Excerpt(s): It has been shown that the neuropeptide, corticotropin releasing factor ("CRF"), acting through its binding to the CRF-1 receptor, is a primary mediator of stress- and anxiety-related physiological responses in humans and other mammals by stimulating ACTH secretion from the anterior pituitary gland. See A. J. Dunn, et al., Brain Res. Rev., 15: 71-100 (1990). Antagonists of the CRF-1 receptor, both peptides (J. Gulvas, et al., Proc. Natl. Acad. Sci. U.S.A., 92: 10575-10579 (1995) and small molecules (J. R. McCarthy, et al., Curr. Pharm. Design, 5: 289-315 (1999), have demonstrated the ability to ameliorate the effects of stressful stimuli in several animal models. In addition, marked elevations of CRF in cerebrospinal fluid have been detected in a large portion of individuals diagnosed with major depression and anxiety disorders, and the levels correlate with severity of the disease. See F. Holsboer, J. Psychiatric Res., 33: 181-214 (1999). Following antidepressant treatment, the increased CRF levels observed in depressed patients were reduced. See C. M. Banki, et al., Eur. Neuropsychopharmacol., 2: 107-113 (1992). CRF has also been shown to be a key mediator of several immune system functions through its effect on glucocorticoid plasma levels. See E. L. Webster, et al., Ann. N.Y. Acad. Sci., 840: 21-62 (1998). Recent reviews of the activity of CRF-1 antagonists, P. J. Gilligan, et al., J. Med. Chem., 43: 1641-1660 (2000) and J. R. McCarthy, et al., Ann. Rep. Med. Chem., 34: 11-20 (1999) are incorporated herein by reference. There appears a need to discover novel small molecule CRF antagonists in order to treat a wide variety of human disorders including depression, anxiety, bipolar disorder, and other stress-related illnesses. See WO 95/10506, WO 95/33750, WO 97/14684, WO 97/35580, WO 98/11075, WO 98/42699, WO 99/01439 and EP 773023. R.sup.5, R.sup.6 and R.sup.7 are each the same or different and selected from the group consisting of H, C.sub.1-6 alkyl, C.sub.1-6 alkoxy, C.sub.1-6 thioalkyl, CN, C.sub.1-6 haloalkyl and halo.

Web site: http://www.delphion.com/details?pn=US06515005\_\_\_

# • Topiramate sodium trihydrate

Inventor(s): Almarsson; Orn (Shrewsbury, MA), Peterson; Matthew L. (Framingham, MA), Remenar; Jules (Framingham, MA)

Assignee(s): Transform Pharmaceuticals, Inc. (Lexington, MA)

Patent Number: 6,559,293

Date filed: September 3, 2002

Abstract: The invention encompasses novel salts of topiramate, and pharmaceutically acceptable polymorphs, solvates, hydrates, dehydrates, co-crystals, anhydrous, or amorphous forms thereof, as well as pharmaceutical compositions and pharmaceutical unit dosage forms containing the same. In particular, the invention encompasses pharmaceutically acceptable salts of topiramate, including without limitation topiramate sodium, topiramate lithium, topiramate potassium, or polymorphs, solvates, hydrates, dehydrates, co-crystals, anhydrous, and amorphous forms thereof. The invention further encompasses novel co-crystals or complexes of topiramate, as well as pharmaceutical compositions comprising them. The invention also encompasses methods of treating or preventing a variety of diseases and conditions including, but not limited to, seizures, epileptic conditions, tremors, cerebral function disorders, obesity, neuropathic pain, affective disorders, tobacco cessation, migraines, and cluster **headache.** 

Excerpt(s): This invention relates to compounds, pharmaceutical compositions, and methods for the treatment or prevention of seizures, epilepsy, tremors, affective disorders, obesity, neuropathic pain, and migraines. Topiramate is a white crystalline powder with a solubility in water of 9.8 mg/mL, and it is freely soluble in acetone, chloroform, dimethylsulfoxide, and ethanol. See, Physician's Desk Reference, 56.sup.th ed., pp. 2590-2595 (2002). Topiramate is sold in the United States under the trade name TOPAMAX.RTM. (Ortho-McNeil Pharmaceutical, Inc., Raritan, N.J., U.S.A.). TOPAMAX.RTM. has been approved for use as an antiepileptic agent as an adjuvant therapy for patients with partial onset seizures, or primary generalized tonic-clonic seizures. See generally, Physician's Desk Reference, 56.sup.th ed., 2590-2595 (2002); see also, U.S. Pat. No. 4,513,006. Adverse effects associated with the administration of topiramate include, but are not limited to, somnolence, dizziness, ataxia, speech disorders and related speech problems, psychomotor slowing, abnormal vision, difficulty with memory, paresthesia, diplopia, renal calculi (kidney stones), hepatic failure, pancreatitis, renal tubular acidosis, acute myopia and secondary angle closure glaucoma. Physician's Desk Reference, 56.sup.th ed., pp. 2590-2595 (2002).

Web site: http://www.delphion.com/details?pn=US06559293\_\_\_

# • Treatment method

Inventor(s): Dedrick; Russell L. (Kensington, CA), Garovoy; Marvin R. (San Anselmo, CA), Kramer; Susan M. (San Francisco, CA), Starko; Karen M. (Hillsborough, CA)

Assignee(s): Genentech, Inc. (South San Francisco, CA), XOMA Technology, Ltd. (Berkeley, CA)

Patent Number: 6,582,698

Date filed: March 28, 2001

Abstract: A method is provided for reducing the occurrence of fever, **headache**, nausea and/or vomiting associated with administration of a therapeutic compound to a mammal in need thereof, comprising administering to the mammal a first conditioning dose of a non-target cell depleting compound which binds to a cell surface receptor on a target mammalian cell; and administering a second therapeutic dose of the compound, wherein the second dose is higher than the first dose.

Excerpt(s): The invention relates to methods of treating mammals, for example humans, to reduce the occurrence of undesired administration reactions, to treat an LFA-1 mediated disease, to condition a mammal to tolerate high doses of a therapeutic compound and to down modulate a cell surface receptor. Administration of many therapeutic agents rapidly induces adverse side effects, or events, including but not limited to fever, headache, nausea, vomiting, breathing difficulties and changes in blood pressure. These adverse events limit the amount of a drug or therapeutic compound that can be given, which in turn limits the therapeutic effectiveness that could be achieved with higher doses of the drug. There is a continuing need to develop techniques which limit the toxicity of higher drug doses so that therapeutic efficacy can be improved. This need exists for both polypeptide and non-polypeptide compounds. Antibodies are one type of polypeptide compound for which there are frequently adverse events upon administration which limit the dose of the compound that can be administered. One compound associated with adverse side effects is the murine monoclonal antibody OKT3. OKT3 binds to the CD3 protein complex that is associated with the T cell receptor (TCR) found on the surface of all T lymphocytes. Administration of OKT3 to humans rapidly reduces the number of circulating T cells (e.g. OKT3 is a cell depleting compound) and reduces the amount of cell surface TCR found on those T cells that remain (Cosimi, et al., 1981 N Engl J Med, 305(6), 308-314). The immunosuppressive effects of OKT3 have been therapeutically useful in the treatment of renal transplant rejection (Goldstein & Group, 1985 M Engl J Med, 313(6), 337-342). However, administration of OKT3 induces a number of adverse side effects, including fever, chills, nausea, vomiting and tightness of chest. These side effects are believed to be caused by cytokine release from T cells due to OKT3-induced activation (Abramowicz, et al., 1989 Transplantation, 47(4), 606-608) and complement activation (Raasveld, et al., 1993 Kidney International, 43 1140-1149).

Web site: http://www.delphion.com/details?pn=US06582698\_\_\_

#### Treatment of migraine, post-traumatic headache, tension-type headaches, atypical facial pain, cervical pain and muscle spasm

Inventor(s): Friedman; Mark (5 Forest Ct., Larchmont, NY 10538)

Assignee(s): none reported

Patent Number: 6,450,170

Date filed: June 15, 2000

Abstract: A new method of treatment of migraine, tension-type **headaches**, posttraumatic **headache**, atypical facial pain as well as cervical pain and muscle spasm is presented, comprising the application of bursts of low power laser light to the area of intra-oral tenderness associated with the above conditions. The zone of tenderness is in the area of the plexus formed by the posterior and middle superior alveolar branches of the ipsilateral maxillary nerve. The intra-oral tenderness associated with migraine, tension-type **headaches**, post-traumatic **headache**, atypical facial pain, cervical pain and muscle spasm disappears almost immediately, returning in approximately 3 hours to a few days, With repeated applications, a marked decrease or elimination of the intra-oral tenderness and similar elimination of migraine, tension-type **headaches**, post-traumatic **headache**, atypical facial pain, cervical and muscle spasm frequency and intensity was observed. The brief application of bursts of low power laser light (non-cutting 5-60 mW) from a low power Helium-Neon, Gallium Arsenide or Gallium Aluminum Arsenide laser, having a maximum output of 60 mW, typically utilizing an application time of 2-15 minutes.

Excerpt(s): The present invention relates to a new method for the treatment of migraine, tension-type headaches, atypical facial pain, post-traumatic headache, cervical pain and muscle spasm. In accordance with the invention, the method of treatment for these headaches, atypical facial pain, cervical pain and muscle spasm comprises the application of low power laser light to the area of intra-oral tenderness which has been found by the inventor herein to be associated with the aforesaid conditions. This zone of tenderness and an increased local temperature are in the area of the plexus formed by the posterior superior alveolar branch of the ipsilateral maxillary nerve. The zone of tenderness is located bilaterally when the symptoms are bilateral and unilaterally when the symptoms are one sided. In the case of tension (muscle contraction) headaches in the frontalis or forehead and/or orbital region, the laser emitted radiation can also be applied to the supraorbital nerve as it emerges from the supraorbital notch or foramen over the eye or at the infraorbital foramen beneath the eye, or at the mandibular foramen in the mandible This laser application is performed either separately or in conjunction with the laser treatment directed to the area of intra-oral tenderness. The intra-oral tenderness associated with migraine, tension-type headaches, post-traumatic headache, cervical muscle spasm and atypical facial pain is markedly decreased or disappears immediately after intra-oral laser application, returning in approximately three hours to a few days, but most importantly it has been found that with repeated applications, the tenderness returns to a lesser degree along with a decrease in symptoms. For the above-noted conditions, a marked decrease or elimination of the above noted conditions' frequency and intensity takes place. Immediate relief is often noted when the patient is symptomatic.

Web site: http://www.delphion.com/details?pn=US06450170\_\_\_
# Patent Applications on Headache

As of December 2000, U.S. patent applications are open to public viewing.<sup>10</sup> Applications are patent requests which have yet to be granted. (The process to achieve a patent can take several years.) The following patent applications have been filed since December 2000 relating to headache:

## • 3,7-dihydro-purine-2,6-dione derivatives as CRF receptor ligands

Inventor(s): Hartz, Richard A.; (Kennett Square, PA)

Correspondence: Stephen B. Davis; Bristol-myers Squibb Company; Patent Department; P O Box 4000; Princeton; NJ; 08543-4000; US

Patent Application Number: 20030119831

Date filed: November 7, 2002

Abstract: Compounds provided herein are 3,7-dihydro-purine-2,6-dione derivatives of Formula (I): 1Such compounds are particularly useful as CRF receptor ligands, and hence, in the treatment of various neurologically-related disorders such as affective disorder, anxiety and depression, **headache**, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis or hypoglycemia.

Excerpt(s): This application claims the priority benefit of U.S. Provisional Appl No. 60/331,829, filed Nov. 20, 2001, the disclosure of which is incorporated herein by reference in its entirety. This invention relates to 3,7-dihydro-purine-2,6-dione derivatives as CRF antagonists, pharmaceutical compositions containing the same, and methods of using the same in the treatment of psychiatric disorders and neurological diseases including affective disorder, anxiety related disorders, depression, headache, post-traumatic stress disorder, supranuclear palsy, Alzheimer's disease, head and spinal cord traumas, anorexia nervosa or other feeding disorders, as well as treatment of irritable bowel syndrome, gastrointestinal diseases, cardiovascular or heart-related diseases, immune supression, human immunodeficiency virus infections, fertility problems, or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF. Corticotropin releasing factor (herein referred to as CRF), a 41 amino acid peptide, is the primary physiological regulator of proopiomelanocortin (POMC)-derived peptide secretion from the anterior pituitary gland [J. Rivier et al., Proc. Nat. Acad. Sci. (USA) 80:4851 (1983); W. Vale et al., Science 213:1394 (1981)]. In addition to its endocrine role at the pituitary gland, immunohistochemical localization of CRF has demonstrated that the hormone has a broad extrahypothalamic distribution in the central nervous system and produces a wide spectrum of autonomic, electrophysiological and behavioral effects consistent with a neurotransmitter or neuromodulator role in brain [W. Vale et al., Rec. Prog. Horm. Res. 39:245 (1983); G. F. Koob, Persp. Behav. Med. 2:39 (1985); E. B. De Souza et al., J. Neurosci. 5:3189 (1985)]. There is also evidence that CRF plays a significant role in integrating the response of the immune system to physiological,

<sup>&</sup>lt;sup>10</sup> This has been a common practice outside the United States prior to December 2000.

psychological, and immunological stressors [J. E. Blalock, Physiological Reviews 69:1 (1989); J. E. Morley, Life Sci. 41:527 (1987)].

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

#### • Amidine derivatives as selective antagonists of ndma receptors

Inventor(s): Curtis, Neil Roy; (Buntingford, GB), Kulagowski, Janusz Jozef; (Sawbridgeworth, GB), Thomas, Steve; (Ware, GB), Watt, Alan Paul; (Great Dunmow, GB)

Correspondence: Merck & Company Inc; 126 East Lincoln Avenue; Rahway; NJ; 07065; US

Patent Application Number: 20030119871

Date filed: December 16, 2002

Abstract: A class of styryl amidine derivatives which are antagonists of the hum NMDA receptor, being selective for those containing the NR2B subunit, are active in the treatment and/or prevention of neurological and neurodegenerative disorders, in particular neuropathic pain and **headache**, specifically migraine, whils displaying fewer ataxic and related side-effects associated with other classes of NMDA receptor antagonists.

Excerpt(s): The present invention relates to a class of amidine derivatives and to their use in the therapy of neurological disorders. In particular, this invention relates to amidines that are useful as selective antagonists of NR2B subunit-containing human Nmethyl-D-aspartate (NMDA) receptors. The compounds of the present invention are thus useful for relieving, treating or preventing neurological and neurodegenerative disorders, including pain (and in particular neuropathic pain and headache, specifically migraine), epilepsy, stroke, anxiety, cerebral ischemia, muscular spasms, Alzheimer's Disease, Huntington's Disease and Parkinson's Disease. Glutamate plays a key role in processes related to chronic pain and pain-associated neurotoxicity, largely acting through NMDA receptors. Much evidence points to the involvement of NMDA receptors in the development and maintenance of neuropathic pain. NMDA receptor antagonists, for example ketamine, dextromethorphan and CPP (3-(2-carboxypiperazin-4-yl)propyl-1-phosphonic acid) have been reported to produce symptomatic relief in a number of neuropathies including postherpetic neuralgia, central pain caused by spinal cord injury and phantom limb pain (Kristensen et al., Pain, 1992, 51, 249-253; Eide et al., Pain, 1995, 61, 221-228; Knox et al., Intensive Care, 1995, 23, 620-622; Max et al., Clin. Neuropharmacol., 1995, 18, 360-368). However, at analgesic doses, psychotomimetic effects that include dizziness, headache, hallucinations, dysphoria and disturbances of cognitive and motor function prohibit their widespread use. To exploit NMDA receptor antagonists as possible treatment options for neuropathic pain, it is necessary to develop new agents with a reduced side-effect profile. Native NMDA receptors are heterodimers composed of an NMDA R1 (NR1) subunit and at least one NMDA R2 (NR2) subunit. Receptor cloning strategies have identified multiple NMDA receptor subunits in the CNS including the NR1 subfamily (with eight isoforms derived from alternative splicing of a single gene) and four NR2 subunits (A, B, C, and D) each encoded by a single gene (for review, see Whiting & Priestley, Frontiers of Neurobiology 3, Amino Acid Neurotransmission, Portland Press, 1996, 153-176). Functional receptors have different physiological and pharmacological properties and are differentially distributed in the mammalian CNS, demonstrating the functional heterogeneity of NMDA receptors (Ishii et al., J. Biol. Chem., 1993, 268, 2836-2843; Wenzel et al., NeuroReport, 1995, 7, 45-48; Laurie et al., Brain Res. Molt Brain Res., 1997, 51, 23-32).

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

## • Apparatus for directed intranasal administration of a composition

Inventor(s): Levin, Bruce H.; (Merion, PA)

Correspondence: Akin Gump Strauss Hauer & Feld L.L.P.; One Commerce Square; 2005 Market Street, Suite 2200; Philadelphia; PA; 19103-7013; US

Patent Application Number: 20030133877

Date filed: August 12, 2002

Abstract: Methods, kits, apparatus, and compositions for inhibiting a cerebral neurovascular disorder, a muscular **headache**, or cerebral inflammation in a human patient are provided. The methods comprise intranasally administering to the patient a pharmaceutical composition comprising a local anesthetic, and preferably a long-acting local anesthetic ingredient. A composition useful for practicing the methods of the invention is described which comprises at least one local anesthetic in a pharmaceutically acceptable carrier, wherein the composition is formulated for intranasal delivery. Cerebral neurovascular disorders include migraine and cluster **headache**. Muscular **headaches** include tension **headaches** and muscle contraction **headaches**. A kit comprising the composition and an intranasal applicator and a method of systemically delivering a pharmaceutically active agent to an animal are also included in the invention. Apparatus for directed intranasal administration of the compositions of the invention and for performing the methods of the invention are also described.

Excerpt(s): This application is a continuation-in-part of U.S. Application Ser. No. 09/492,946, filed Jan. 27, 2000, which is entitled to priority pursuant to 35 U.S.C.sctn.119(e) to U.S. Provisional Application No. 60/117,398, filed Jan. 27, 1999, a continuation-in-part of U.S. Application Ser. No. 09/737,302, filed Dec. 15, 2000, which is entitled to priority pursuant to 35 U.S.C.sctn.119(e) to U.S. Provisional Application No. 60/170,817, filed Dec. 15, 1999, and a continuation-in-part of U.S. Application No. 60/170,817, filed Dec. 15, 1999, and a continuation-in-part of U.S. Application No. 09/118,615, filed Jul. 17, 1998, which is entitled to priority pursuant to 35 U.S.C.sctn.119(e) to U.S. Application Ser. No. 08/897,192, filed Jul. 21, 1997, converted to U.S. Provisional Application No. 60/072,845, filed Jan. 28, 1998, and to U.S. Provisional Application No. 60/084,559, filed May 6, 1998. Not applicable.

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

## Aromatic and heteroaromatic substituted amides

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Patent Application Number: 20030064983

Date filed: July 17, 2002

Abstract: The invention is the compounds2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1dioxo-1.lambda.sup.6-thiomorpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methyland2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1.lambda.sup.6isobutyramide pholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyrathiomormide.Compounds of the invention are useful in pharmaceutical compositions for the treatment of migraine, rheumatoid arthritis, asthma, bronchial hyperreactivity, inflammatory bowel disease or for the treatment of disorders including Parkinson's disease, anxiety, depression, pain, headache, Alzheimer's disease, multiple sclerosis, edema, allergic rhinitis, Crohn's disease, ocular injury, ocular inflammatory diseases, psychosis, motion sickness, induced vomiting, emesis, urinary incontinence, psychoimmunologic or psychosomatic disorders, cancer, withdrawal symptoms of addictive drugs from opiates or nicotine, traumatic brain injury or benign prostatic hyperplasia.

Excerpt(s): R.sup.1 is selected from the group consisting of hydrogen and fluoro. Compounds of formula 1, and pharmaceutically acceptable acid addition salts thereof, have been shown to mediate the Neurokinin 1 (NK-1, substance P) receptor. The neuropeptide receptor for substance P (NK-1) is widely distributed throughout the mammalian nervous system (especially brain and spinal ganglia), the circulatory system and peripheral tissues (especially the duodenum and jejunum) and are involved in regulating a number of diverse biological processes. The receptor for substance P is a member of the superfamily of G protein-coupled receptors. The central and peripheral actions of the mammalian tachykinin substance P have been associated with numerous inflammatory conditions including migraine, rheumatoid arthritis, asthma, and inflammatory bowel disease as well as mediation of the emetic reflex and the modulation of central nervous system (CNS) disorders such as Parkinson's disease (Neurosci. Res., 1996, 7, 187-214), anxiety (Can. J. Phys., 1997, 75, 612-621) and depression (Science, 1998, 281, 1640-1645).

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

# Branched chain amino acid-dependent aminotransferase inhibitors and their use in the treatment of neurodegenerative diseases

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Patent Application Number: 20030149110

Date filed: November 26, 2002

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Abstract: The invention relates to BCAT inhibitors and the use thereof for treating or preventing neuronal loss associated with stroke, ischemia, CNS trauma, hypoglycemia and surgery, as well as treating neurodegenerative diseases including Alzheimer's disease, amyotrophic lateral sclerosis, Huntington's disease and Down's syndrome, treating or preventing the adverse consequences of the overstimulation of the excitatory amino acids, treating anxiety, psychosis, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine **headache**, chronic pain, neuropathic pain, Parkinson's disease, diabetic retinopathy, glaucoma, CMV retinitis, urinary incontinence, opioid tolerance or withdrawal, and inducing anesthesia, as well as for enhancing cognition.

Excerpt(s): This application claims benefit of U.S. Provisional Application No. 60/333,636 filed Nov. 27, 2001. This invention is related to branched chain amino aciddependent amino transferase (BCAT) inhibitors. The invention is also directed to the use of BCAT inhibitors as neuro-protective agents for treating conditions such as stroke, cerebral ischemia, central nervous system trauma, hypoglycemia, anxiety, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine headaches, chronic pain, neuropathic pain, glaucoma, CMV retinitis, diabetic retinopathy, psychosis, urinary incontinence, opioid tolerance or withdrawal, or neuro-degenerative disorders such as lathyrism, Alzheimer's disease, Parkinsonism, amyotrophic lateral sclerosis (ALS), and Huntington's Disease. Excessive excitation by neurotransmitters can cause the degeneration and death of neurons. It is believed that this degeneration is in part mediated by the excitotoxic actions of the excitatory amino acids (EAA) glutamate and aspartate at the N-methyl-D-aspartate (NMDA) receptor. This excitotoxic action is considered responsible for the loss of neurons in cerebrovascular disorders such as cerebral ischemia or cerebral infarction resulting from a range of conditions, such as thromboembolic or hemorrhagic stroke, cerebral vasospasms, hypoglycemia, cardiac arrest, status epilepticus, perinatal asphyxia, anoxia such as from drowning, pulmonary surgery and cerebral trauma, as well as lathyrism, Alzheimer's disease, Parkinson's disease, and Huntington's disease.

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

• Carbamate compounds for use in preventing or treating neuropathic pain and cluster and migraine headache-associated pain

Inventor(s): Codd, Ellen E.; (Blue Bell, PA), Plata-Salaman, Carlos R.; (Ambler, PA), Rogers, Katherine E.; (Audobon, PA), Shank, Richard P.; (Blue Bell, PA), Zhao, Boyu; (Lansdale, PA)

Correspondence: Audley A. Ciamporcero JR.; Johnson & Johnson; One Johnson & Johnson Plaza; New Brunswick; NJ; 08933-7003; US

Patent Application Number: 20020107283

Date filed: July 16, 2001

Abstract: This invention is directed to a method for preventing or treating neuropathic pain and cluster and migraine headache-associated pain comprising administering to a subject in need thereof a therapeutically effective amount of an enantiomer of Formula (I) substantially free of other enantiomers or an enantiomeric mixture wherein an enantiomer of Formula (I) predominates: 1wherein phenyl is substituted at X with one to five halogen atoms independently selected from the group consisting of fluorine, chlorine, bromine and iodine; and; R.sub.1 and R.sub.2 are independently selected from the group consisting of hydrogen and C.sub.1-C.sub.4 alkyl; wherein C.sub.1-C.sub.4 alkyl is optionally substituted with phenyl (wherein phenyl is optionally substituted with substituents independently selected from the group consisting of hydrogen, halogen, C.sub.1-C.sub.4 alkyl, C.sub.1-C.sub.4 alkoxy, amino, nitro and cyano).

Excerpt(s): This patent application claims benefit of U.S. patent application Ser. No. 60/219,657 filed on Jul. 21, 2000, which is hereby incorporated by reference. This invention is directed to a method for use of a carbamate enantiomer in preventing or treating neuropathic pain and cluster and migraine headache-associated pain. More particularly, this invention is directed to a method for use of a halogenated 2-phenyl-1,2-ethanediol monocarbamate enantiomer substantially free of other enantiomers for preventing or treating neuropathic pain and cluster and migraine headache-associated

pain. The conditions grouped under the term neuropathic pain constitute an area of continuing medical need.

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

#### Certain pyrrolopyridine derivatives: novel CRF1 specific ligands

Inventor(s): Horvath, Raymond F.; (Guilford, CT), Hutchison, Alan; (Madison, CT)

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Patent Application Number: 20020111490

Date filed: March 12, 2002

Abstract: Disclosed are compounds of the formula: 1whereinAr is optionally substituted aryl or heteroarylR.sub.1 is hydrogen or alkyl;R.sub.7 is hydrogen or alkyl;R.sub.2 is hydrogen, halogen, alkyl or alkoxy; orR.sub.1 and R2 taken together with the ring to which they are attached form a 5-9 membered saturated or aromatic ring optionally having a hetero atom selected from oxygen, sulfur or nitrogen;R.sub.3 and R.sub.4 are independently hydrogen, alkyl, cycloalkyl, aryl or heteroaryl groups; orR.sub.3 and R.sub.4 are independently in heteroaryl groups; orR.sub.3 and R.sub.4 together with the nitrogen atom to which they are attached form a 5-8 membered ring; andR.sub.5 is hydrogen, halogen, straight or branched chain lower alkyl having 1-6 carbon atoms, or straight or branched chain lower alkoxy or thioalkoxy having 1-6 carbon atoms, which compounds are highly selective partial agonists or antagonists at human Corticotropin-Releasing Factor 1 (CRF1) receptors and are useful in the diagnosis and treatment of treating stress related disorders such as post trumatic stress disorder (PTSD) as well as depression, **headache** and anxiety.

Excerpt(s): This invention relates to novel substituted pyrrolopyridine derivatives which selectively bind to Corticotropin-Releasing Factor (CRF) receptors. More specifically, it relates to tetrahydro-5H-pyrido[2,- 3-b]indol-4-amines, 9H-pyrido[2,3-b]indol-4-amines, and 1H-pyrrolo[2,3-b]pyridin-4-amines, and their use as antagonists of Corticotropin-Releasing Factor in the treatment of various disease states. Corticotropin-releasing factor (CRF) antagonists are mentioned in U.S. Pat. Nos. 4,605,642 and 5,063,245 referring to peptides and pyrazoline derivatives, respectively. The importance of CRF antagonists is described in the literature, for example, as discussed in U.S. Pat. No. 5,063,245, which is incorporated herein by reference in its entirety. CRF antagonists are considered effective in the treatment of a wide range of diseases including stress-related illnesses, such as stress-induced depression, anxiety, and **headache**. Other diseases considered treatable with CRF antagonists are discussed in U.S. Pat. No. 5,063,245 and Pharmin. Rev., 43: 425-473 (1991). International application WO 9413676 A1 discloses pyrrolo[2,3-d]pyrimidines as having Corticotropin-Releasing Factor antagonist activity. J. Het. Chem. 9, 1077 (1972) describes the synthesis of 9-Phenyl-pyrrolo[3,2-d]pyrimidines.

# • Clever frame/clip

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Patent Application Number: 20030090621

Date filed: October 25, 2002

Abstract: For the eyewear products, currently the most popular clip-on of sun glasses is the magnetic clip, which is non-reliable after using a period of time. It's also said the magnetic pieces would cause **headache** to some people. This invention is try to offer a reliable mechanic structure to the frame/clip to facilitate people who wear glasses.

Excerpt(s): These years magnetic easy frame/clip is very popular among people wearing glasses. Though easy to use when it's new, it'd become non-reliable after using a period of time. Also it's said the magnitic pieces would cause **headache** to some groups of people. This invention is to offer a new frame/clip which is mechanic structure and easy to use, reliable while matching various kinds of styles of designs. The above description includes the parts on one side, let's say, the right side covering the right eye. For the other side, the left side covering the left eye, the same parts would be at the same symmetrical positions.

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

# • Compositions and methods for enhancing analgesic potency of tramadol and attenuating its adverse side effects

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Patent Application Number: 20030148941

Date filed: March 12, 2002

Abstract: The invention generally relates to compositions and methods with tramadol and an opioid antagonist to enhance analgesic potency and/or attenuate one or more adverse effects of tramadol, including adverse side effect(s) in humans such as nausea, vomiting, dizziness, **headache**, sedation (somnolence) or pruritis. This invention relates to compositions and methods for selectively enhancing the analgesic potency of tramadol and simultaneously attenuating anti-analgesia, hyperalgesia, hyperexcitability, physical dependence and/or tolerance effects associated with the administration of tramadol. The methods of the present invention comprise administering to a subject an analgesic or subanalgesic amount of tramadol and an amount of excitatory opioid receptor antagonist such as naltrexone or nalmefene effective to enhance the analgesic potency of tramadol and attenuate the anti-analgesia, hyperalgesia, hyperexcitability, physical dependence and/or tolerance effects of tramadol.

Excerpt(s): This is a continuation-in-part of co-pending application Ser. No. 09/306,164 filed May 6, 1999, the content of which is hereby incorporated by reference in its entirety. Morphine or other bimodally-acting opioid agonists are administered to relieve severe pain due to the fact that they have analgesic effects mediated by their activation

of inhibitory opioid receptors on nociceptive neurons (see North, Trends Neurosci., Vol. 9, pp. 114-117 (1986) and Crain and Shen, Trends Pharmacol. Sci., Vol. 11, pp. 77-81 (1990)). However, morphine and other bimodally-acting opioid agonists also activate opioid excitatory receptors on nociceptive neurons, which attenuate the analgesic potency of the opioids and result in the development of physical dependence and increased tolerance (see Shen and Crain, Brain Res., Vol. 597, pp. 74-83 (1992)), as well as hyperexcitability, hyperalgesia and other undesirable (excitatory) side effects. As a result, a long-standing need has existed to develop a method of both enhancing the analgesic (inhibitory) effects of bimodally-acting opioid agonists and blocking or preventing undesirable (excitatory) side effects caused by such opioid agonists. Tramadol is an orally active, clinically effective, centrally acting analgene compound with opioid and non-opioid activity. This synthetic analgesic has a novel mechanism of action involving a complementary and synergistic interaction between inhibition of neuronal monamine uptake and weak affinity for opioid receptors (Raffa et al., Rev. Contemp. Pharmacother. 6:485-497 (1995)). Tramadol is generally well tolerated, with dizziness, nausea, constipation, headache, somnolence (sedation), vomiting, pruritis, CNS stimulation, sezures, asthenia, dyspepsia, diarrhea, dry mouth and/or sweating as adverse side effects. Respiratory depression is uncommon (Lee et al., Drugs 46: 313-340 (1993); Vickers et al., Anaesthesia 47: 291-296 (1992)). Tramadol is marketed in the United States as ULTRAM.RTM. Data from a double-blind, crossover study suggest that oral tramadol 120 mg is equipotent to oral morphine 30 mg (Wilder et al., Ann. Oncol. 5: 141-146 (1994)). A need thus exists for compositions and methods that could enhance the analgesic potency of tramadol and/or block or prevent its adverse side effects, particularly its principal adverse effects in humans.

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

#### Cytokine antagonists for neurological and neuropsychiatric disorders

Inventor(s): Tobinick, Edward Lewis; (Los Angeles, CA)

Correspondence: Ezra Sutton, ESQ.; Ezra Sutton, P.A.; Plaza 9; 900 Route 9; Woodbridge; NJ; 07095; US

Patent Application Number: 20030049256

Date filed: October 9, 2002

Abstract: Methods for treating neurological or neuropsychiatric diseases or disorders in humans by administering to the human a therapeutically effective dose of specific biologics are presented. The biologics of consideration include antagonists of tumor necrosis factor or of interleukin-1. The administration of these biologics is performed by specific methods, most, but not all of which fall into the category of anatomically localized administration designed for perispinal use. Anatomically localized administration involving perispinal use includes, but is not limited to the subcutaneous, intramuscular, interspinous, epidural, peridural, parenteral or intrathecal routes. Additonally, intranasal administration is discussed as a method to provide therapeutic benefit.The clinical conditions of consideration include, but are not limited to the following: diseases of the brain, including neurodegenerative diseases such as Alzheimer's Disease and Parkinson's Disease; migraine **headache**; spinal radiculopathy associated with intervertebral disc herniation, post-herpetic neuralgia, reflex sympathethic dystrophy, neuropathic pain, vertebral disc disease, low back pain, amyotrophic lateral sclerosis, chronic fatigue syndrome; and neuropsychiatric diseases, including bipolar affective disorder, anorexia nervosa, nicotine withdrawal, narcotic addiction, alcohol withdrawl, postpartum depression, and schizoaffective illness.

Excerpt(s): This is a continuation-in-part of application Ser. No. 10/236,097, filed on Sep. 6, 2002, which is a continuation-in-part of application Ser. No. 09/841,844, filed on Apr. 25, 2001, which is a continuation-in-part of application Ser. No. 09/826,976, filed on Apr. 5, 2001, now U.S. Pat. No. 6,419,944, which is a continuation-in-part of application Ser. No. 09/563,651, filed on May 2, 2000, which is a continuation-in-part of application Ser. No. 09/476,643, filed on Dec. 31, 1999, now U.S. Pat. No. 6,177,077, which is a continuation-in-part of application Ser. No. 09/275,070, filed on Mar. 23, 1999, now U.S. Pat. No. 6,015,557, which is a continuation-in-part of application Ser. No. 09/256,388, filed on Feb. 24, 1999, now abandoned. The present invention relates to novel methods of use of specific cytokine antagonists for the treatment of neuropsychiatric and neurological disorders in humans. More particularly, these cytokine antagonists are used in a new treatment of neuropsychiatric and neurologic diseases and disorders, including, but not limited to affective disorders, including unipolar and bipolar affective disorders; schizoaffective illness, schizophrenia, autism, depression, anorexia nervosa, obsessive-compulsive disorders, narcotic addiction, and smoking cessation/nicotine withdrawal; diseases and disorders of the brain; neurodegenerative disorders, including but not limited to Parkinson's Disease and Alzheimer's Disease; spinal cord injury, amyotrophic lateral sclerosis; headache syndromes, including, but not limited to migraine headaches and cluster headaches; neurologic disorders associated with neuropathic pain, including, but not limited to lumbar and cervical radiculopathy, low back pain, vertebral disc disease, fibromyalgia, post-herpetic neuralgia, and reflex sympathetic dystrophy; and chronic fatigue syndrome; utilizing specific anatomic methods of administration of these specific biologics. The delivery of these cytokine antagonists is performed by specific methods, most of which fall into the categories of perispinal administration or intranasal administration. Perispinal administration involves an anatomically localized injection performed so as to deliver the therapeutic molecule directly into the vicinity of the spine. Perispinal administration includes, but is not limited to the subcutaneous, intramuscular, interspinous, epidural, peridural, parenteral, or intrathecal routes, and may be perilesional or alternatively, particularly when treating diseases of the brain, remote from the ultimate site of pathology. Intranasal administration includes the delivery of these particular cytokine antagonists by instillation into the nasal passages, either by nasal spray or nasal inhaler. The cytokine antagonists of consideration are those designed to block the action of, inhibit, or antagonize the biologic effects of tumor necrosis factoralpha (TNF) or interleukin-1 (IL-1). These antagonists may take the form of a fusion protein (such as etanercept); a monoclonal antibody (such as infliximab); a binding protein (such as onercept; Serono); an antibody fragment (such as CDP 870, Pharmacia); or other types of molecules which are potent, selective, and specific inhibitors of the action of these proinflammatory cytokines and are capable of being used by parenteral injection. Localized administration for the treatment of localized clinical disorders has many clinical advantages over the use of conventional systemic treatment. Locally administered medication after delivery diffuses through local capillary, venous, arterial, and lymphatic action to reach the anatomic site of pathology, or, alternatively, to reach the cerebrospinal fluid (CSF). In addition local administration of a biologic in the vicinity of the spine (perispinal administration) has the key advantage of improved delivery of the agent to the central nervous system (CNS). Local intranasal administration of a biologic is another method to improve delivery of the biologic to the CNS, and is discussed here as a method to treat neuropsychiatric disorders, including disorders of mood (depression, bipolar disorder) utilizing TNF antagonists or IL-1 antagonists.

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

• Cytotoxin (non-neurotoxin) for the treatment of human headache disorders and inflammatory diseases

Inventor(s): Borodic, Gary E.; (Canton, MA)

Correspondence: Michael N. Nitabach; Milbank, Tweed, Hadley & Mccloy Llp; 1 Chase Manhattan Plaza; New York; NY; 10005; US

Patent Application Number: 20020187164

Date filed: August 5, 2002

Abstract: Pharmaceutical applications of a chemodenervating agent reduce pain by altering release of pain- and inflammation-mediating autocoids, with a duration of action between 12-24 weeks. The limiting factor in dosing for this application is weakness and paralysis created by higher doses of the chemodenervating pharmaceutical mediated by action of the neurotoxin component of this chemodenervating pharmaceutical. The invention described herein represents a novel mechanism and pharmaceutical formulation which eliminates the neurotoxin component of the chemodenervating pharmaceutical, while retaining the cytotoxin component which provides an essential bioeffect for the relief of pain and inflammation. The invention allows for improvement in administering the pharmaceutical agent for the reduction of pain and/or inflammation without causing muscular weakness and paralysis.

Excerpt(s): I claim priority to U.S. patent application Ser. No. 09/458,784, filed Dec. 10, 1999, and hereby incorporate said application by reference herein in its entirety. This invention relates to the composition of chemodenervating agents used for the treatment of diseases. The invention offers an improvement on the prior art by eliminating the muscle-weakening side effect of prior-art chemodenervating agents. This is achieved by eliminating the neurotoxin component of the chemodenervating agent. Migraine and tension **headaches** are a major cause of loss of productivity for those afflicted, usually due to pain and associated systemic symptoms. The syndrome of migraine and other essential **headaches** is characterized by severe throbbing **headaches** often made worse by physical activity and associated with aversion to light and sound. The syndrome often, but not always, includes nausea and/or sometimes vomiting as major components. The pain is often unilateral or localized to a portion of the head. The condition is episodic in nature, with episodes typically lasting 4-72 hours.

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

• Galenical preparations of dapsone and related sulphones, and method of therapeutic and preventative treatment of disease

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Patent Application Number: 20030092635

Date filed: August 26, 2002

Abstract: Dapsone and related sulfones are known to have therapeutic activity against leprosy, dermatitis herpetiformis, actinomycotic mycetoma, asthma, malaria, rheumatoid arthritis, Kaposis sarcoma, pneumocystis carini (pneumonia), subcorneal pustular dermatosis and cystic acne, in patients in need of such therapy. These sulfones are also known to have therapeutic activity against memory loss in patients in need of such therapy, including patients suffering from Alzheimer's disease and related neurodegenerative disorders. It has now been found that new, modified-release formulations of dapsone and related sulfones may also be used that decrease side effects and increase effectiveness of the drugs. New methods are disclosed utilizing certain formulations of dapsone and related sulfones that improve the therapeutic index of said drugs. Side effects of these drugs are known to those skilled in the art and include, but are not restricted to anorexia, psychosis, agranulocytosis, peripheral neuritis, hemolysis, methemoglobinemia, nausea, vomiting, headache, dizziness, tachycardia, nervousness, insomnia and skin disorders. Modified-release (as defined herein) formulations of dapsone have now been found to avoid some or all of these side effects, and to have more efficacy on potency.

Excerpt(s): The object of the present invention pertains to a method of treating or preventing certain diseases in a human being while increasing compliance, reducing side effects and improving efficacy of the active therapeutic ingredient(s) within a large therapeutic range. The method comprises the use of modified-release dosage formulations of sulfone compounds including 4,4'-diaminodiphenylsulfone, its didextrose sulfonate derivative(s), their analogs, metabolites, any enantiomers, any diasteriomers, or mixtures thereof and/or therapeutically acceptable salts thereof. Dapsone is an active substance that is known in the treatment of various infectious diseases and inflammatory conditions. There is a wealth of data and experimental studies regarding the activity of dapsone and related sulfones. In particular, there is a large amount of data regarding the bioavailability and pharmacokinetics of the drug. It is also known in the prior art that dapsone has therapeutic activity against leprosy, dermatitis herpetiformis, actinomycotic mycetoma, asthma, malaria, rheumatoid arthritis, Kaposis sarcoma, pneumocystis carinii (pneumonia), subcorneal pustular dermatosis and cystic acne, in patients in need of such therapy. However, since the acute or chronic toxicity of dapsone is unacceptable at the doses necessary to treat most diseases, it is not possible to use this compound for these indications in the presently available formulation(s).

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

## Hair dryer

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Patent Application Number: 20030196344

Date filed: April 22, 2003

Abstract: Disclosed is the hair dryer. In the hair dryer, a hollow dryer housing has an inlet port, an outlet port and a front handle. An intake cover is coupled to a rear side of the dryer housing and has a rear handle protruding downwardly from the hollow dryer, for suctioning an outer air into the dryer housing. A nozzle is coupled to the outlet port of the dryer housing. A heating assembly is positioned in the dryer housing and in the intake cover, and includes a hollow assembly body, a support frame, a driving motor, a

rotating shaft, and a blowing fan. A shielding member is installed along an inner side of the dryer housing, the intake cover, and the nozzle. Due to this structure, the hair dryer is capable of absorbing and shielding the magnetic wave not to cause human problems such as **headache**, dermatitis and chronic fatigue.

Excerpt(s): The present invention relates to a hair dryer, more particularly, it relates to a hair dryer having a shielding function against magnetic wave, which is used for drying and styling hair. The hair dryer 100 further comprises a heating assembly 140 that is installed at the interior of the dryer housing 110 and the intake cover 120. The heating assembly 140 has an assembly body 142, a driving motor 144, and a blowing fan 148. A support frame 144 protrudes from the front side of the assembly body 142. The driving motor 146 is mounted on the interior of the assembly body 142, and a part of which is inserted into the support frame 144. A rotation shaft (not shown) projects out of the rear side of the driving motor 146. The blowing fan 148 is forcibly inserted into the rotation shaft (not shown) of the driving motor (146) so that the blowing fan 148 blows an outside air out of the inlet port 112 to the outlet port 114 by the rotation of the driving motor 146. Further, the hair dryer 100 includes an electrical cord 150, an electrical switch 152, and a heating wire 154. The electrical cord 150 supplies an electrical power to the driving motor 146. The electrical switch 152 is connected to the electrical cord 150, which controls the opening and closing of the electrical power. The heating wire 154 winds around the support frame 144 for heating a sucked air through the inlet port 112 of the dryer housing 110.

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

### • Imidazolyl derivatives as corticotropin releasing factor inhibitors

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Correspondence: Stephen B. Davis; Bristol-myers Squibb Company; Patent Department; P O Box 4000; Princeton; NJ; 08543-4000; US

Patent Application Number: 20020183375

Date filed: January 11, 2002

Abstract: The present invention relates to novel heterocyclic antagonists of Formula (I) and pharmaceutical compositions comprising said antagonists of the corticotropin releasing factor receptor ("CRF receptor") 1useful for the treatment of depression, anxiety, affective disorders, feeding disorders, post-traumatic stress disorder, **headache**, drug addiction, inflammatory disorders, drug or alcohol withdrawal symptoms and other conditions the treatment of which can be effected by the antagonism of the CRF-1 receptor.

Excerpt(s): This non-provisional application claims priority from provisional application U.S. Ser. No. 60/264,570 filed Jan. 26, 2001. The present invention relates to antagonists and pharmaceutical compositions comprising said antagonists of the corticotropin releasing factor receptor ("CRF receptor") useful for the treatment of depression, anxiety, affective disorders, feeding disorders, post-traumatic stress disorder, **headache**, drug addiction, inflammatory disorders, drug or alcohol withdrawal symptoms and other conditions the treatment of which can be effected by the antagonism of the CRF-1 receptor. It has been shown that the neuropeptide, corticotropin releasing factor ("CRF"), acting through its binding to the CRF-1 receptor, is a primary mediator of stress- and

anxiety-related physiological responses in humans and other mammals by stimulating ACTH secretion from the anterior pituitary gland. See A. J. Dunn, et al., Brain Res. Rev., 15: 71-100 (1990). Antagonists of the CRF-1 receptor, both peptides (J. Gulyas, et al., Proc. Natl. Acad. Sci. U.S.A., 92: 10575-10579 (1995) and small molecules (J. R. McCarthy, et al., Curr. Pharm. Design, 5: 289-315 (1999), have demonstrated the ability to ameliorate the effects of stressful stimuli in several animal models. In addition, marked elevations of CRF in cerebrospinal fluid have been detected in a large portion of individuals diagnosed with major depression and anxiety disorders, and the levels correlate with severity of the disease. See F. Holsboer, J. Psychiatric Res., 33: 181-214 (1999). Following antidepressant treatment, the increased CRF levels observed in depressed patients were reduced. See C. M. Banki, et al., Eur. Neuropsychopharmacol., 2: 107-113 (1992); see also Effects of the high-affinity corticotropin-releasing hormone receptor 1 antagonist R121919 in major depression: the first 20 patients treated. Zobel A W, Nickel T, Kunzel H E, Ackl N, Sonntag A. Ising M, Holsboer F J Psychiatr Res 2000, 34, 171-181. CRF has also been shown to be a key mediator of several immune system functions through its effect on glucocorticoid plasma levels. See E. L. Webster, et al., Ann. N.Y. Acad. Sci., 840: 21-32 (1998). Recent reviews of the activity of CRF-1 antagonists include P. J. Gilligan, et al., J. Med. Chem., 43: 1641-1660 (2000) and J. R. McCarthy, et al., Ann. Rep. Med. Chem., 34: 11-20 (1999). There appears a need to discover novel small molecule CRF antagonists in order to treat a wide variety of human disorders including depression, anxiety, bipolar disorder, and other stress-related illnesses. See WO 98/35967, WO 99/01454, WO 99/10350, wo 99/67247, 00/01675, WO 00/01697, WO 00/39127, WO 00/59907, WO 00/59908, EP 778277, EP 812831.

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

# • Intraoral discluder device and method for preventing migraine, tension headache, and temporomandibular disorders

Inventor(s): Boyd, James P. SR.; (Solana Beach, CA)

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Patent Application Number: 20030116164

Date filed: December 14, 2001

Abstract: A semi-custom intraoral discluder device for preventing chronic tension and common migraine **headaches** and temporomandibular disorders that are caused or perpetuated by chronic activity of the temporalis muscle. The discluder includes a trough, contoured to encompass at least one maxillary or mandibular incisor, from which extends a protrusion, typically of a dome shape. The trough can be retained on the teeth by any adaptable material which can flow around the teeth and then maintain its shape. The adaptation of the retentive material can be performed by the end user, health care provider, or anyone trained in the art. Once in place in the wearer's mouth, one or two opposing incisor teeth will come into contact with the protrusion prior to the upper and lower posterior and/or canine teeth coming into contact, regardless of the position of the mandible, thereby reducing the intensity of the activity of the temporalis muscle.

Excerpt(s): The present invention relates generally to intraoral devices and, more particularly, to an intraoral discluder device for use in relieving tension and common migraine **headaches** and temporomandibular disorders. Tension and muscle contraction **headaches** affect many people every day. The **headaches** are often recurring and,

without effective treatment, can become very painful, restricting an individual's ability to think clearly and function effectively. The discomfort associated with tension and muscle contraction **headaches** is usually due to pain from strained and fatigued muscles of the head. The majority of the muscles of the human head are not sufficiently strong to elicit the type of pain and discomfort associated with tension and muscle contraction **headaches**. That is not the case with the temporalis muscle, however, which is located on the side of the skull and extends from just behind the eye to just behind the ear, and which is an extremely powerful muscle that functions to close or elevate the jaw. Under normal circumstances, the temporalis muscle should not exert a large static force by contracting isometrically, except possibly during normal chewing. Inappropriate isometric contraction of temporalis muscle is commonly known as "clenching" and clinically known as myofascial dysfunction. Unfortunately, myofacial dysfunction is particularly difficult to detect or diagnose because the act of clenching is a relatively motionless act that is commonly done while a person is concentrating on another topic, or while sleeping.

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

#### Intravenous valproate for acute treatment of migraine headache

Inventor(s): Edwards, Keith R.; (Williamstown, MA)

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Patent Application Number: 20020156131

Date filed: December 27, 2001

Abstract: The present invention features a novel therapy for effecting acute treatment of migraine **headache**. The therapy involves intravenous administration of valproate and is equal to and in some respects superior to previously-known therapies for abortive treatment of prolonged moderate to severe acute migraine **headache**.

Excerpt(s): This application claims the benefit of prior-filed U.S. Provisional Patent Application Serial No. 60/132,416, entitled "Intravenous Valproate for Acute Treatment of Migraine Headache", filed May 4, 1999 (pending). The content of the referenced application is incorporated herein by reference. Migraine headache is a chronic and disabling condition affecting a significant portion of the population throughout the world. The pharmacologic management of migraine has traditionally focused on two approaches: symptomatic or acute treatment and prophylactic therapy. The objective of acute treatment is to reduce the intensity and duration of pain with its attendant symptoms and to optimize the patient's ability to function normally whereas the major objective of prophylactic therapy is the reduction of frequency, duration, and intensity of attacks. A variety of treatment strategies are available for the prophylactic treatment of migraines including beta-blocking drugs (e.g., propranolol), amitriptyline, flunarizine, serotonin antagonists (e.g., methysergide) and nonsteroidal antiinflammatory drugs (e.g., naproxen) are the major classes of agents that have been used in the prophylactic treatment of migraines. See e.g., Deleu et al (1998) Clin. Neuropharmacol. 21:267-79 for review. Strategies for the acute treatment of migraines are also known which generally involve the use of simple analgesics, nonsteroidal antiinflammatory drugs, antiemetics, narcotic analgesics, ergot derivatives, or serotoninagonists, either alone or in combination. For example, dihydroergotamine (DHE) has been used for several decades for treatment of acute migraine headache and produces good relief in 70-80% of subjects at 2 hours after administration (Callaham and Raskin (1986) Headache 26;168-171). Sumatriptan produces similar efficacy, as do several newer

serotonin 1B/1D receptor agonists (Cady et al. (1991) JAMA 265:2831-2835; Mathew et al. (1992) Arch Neurol. 49:1271-1276 and Rapoport (1997) **Cephalalgia** 17: 464-465).

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

### • Method for diagnosis of chronic headache

Inventor(s): Almazov, Irina G.; (Kfar Saba, IL)

Correspondence: DR. Mark Friedman Ltd; C/o Bill Polkinghorn - Discovery Dispatch; 9003 Florin Way; Upper Marlboro; MD; 20772; US

Patent Application Number: 20020179095

Date filed: May 29, 2001

Abstract: A method for determining a cause of chronic **headache** is disclosed. The method includes: (a) determining whether the **headache** of a person is postural, (b) determining whether the person has meningeal irritation, and (c) determining that the **headache** is caused by intracranial hypotension if the **headache** is postural and the person has meningeal irritation.

Excerpt(s): The present invention relates to clinical medical diagnosis and, more particularly, to a method for determining a cause of chronic **headache**. Headache is felt to be the most common human malady and the most prevalent neurologic symptom associated with any disease. Without question, the most frequent of all the painful states that afflict humans, it rivals backache as the most common reason for medical consultation. It accounts for almost 20 million outpatient visits a year in the United States. and is a leading cause for the use of over-the-counter medications. Headache is a major social and economic burden for society. In children, **headache** is an extremely common complaint. Depending on the etiology, frequency and intensity of the **headache**, **headaches** can have a major effect on a child's school attendance and academic performance, as well as the child's memory, personality and interpersonal relationships.

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

### Method of relieving migraines or headaches

Inventor(s): Bertolucci, Lawrence E.; (Carlsbad, CA)

Correspondence: Crockett & Crockett; Suite 400; 24012 Calle DE LA Plata; Laguna Hills; CA; 92653; US

Patent Application Number: 20020138116

Date filed: March 21, 2001

Abstract: A device for providing noninvasive electrical stimulation of a single acupuncture site for treatment of migraines and/or **headaches** is disclosed.

Excerpt(s): The methods and devices described below relate to the fields of treatment of migraines and/or **headaches** and noninvasive electrical stimulation of an acupuncture point. A **headache** is pain that occurs in the tissues covering the brain, the attaching structures at the base of the brain, and the muscles and blood vessels around the scalp, face, and neck. The three most common **headaches** are tension, migraine, and cluster. Tension **headaches** are the most common and cluster **headaches** affect only about one-

percent of the population, mostly males. The exact mechanism for each type of **headache** is not known. Some experts theorize that they all occur from the same mechanism. Migraines are divided into two types, the common migraine and the classical migraine. The difference between the common and the classical migraine is whether or not the patient experiences the migraine aura prior to experiencing the **headache**. The migraine aura is a composite of possible symptoms, namely, visual disturbances, light sensitivity, speech difficulty, tingling of the face or hands, and confusion. The common migraine is not preceded by an aura, while the classical migraine is preceded by an aura.

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

#### Method of treatment

Inventor(s): Gupta, Paul; (Sandwich, GB), Jones, Shirley; (Sandwich, GB), Lahuerta, Juan; (Sandwich, GB), Land, Gillian Christine; (Sandwich, GB), Monkhouse, Kathryn Louis; (Sandwich, GB), Robson, Susan Frances; (Sandwich, GB), Samuels, Gillian Mary; (Sandwich, GB), Wilson, Alan Brian; (Sandwich, GB), Wythes, Martin James; (Sandwich, GB)

Correspondence: Pfizer Inc; 150 East 42nd Street; 5th Floor - Stop 49; New York; NY; 10017-5612; US

Patent Application Number: 20030055098

Date filed: August 12, 2002

Abstract: The invention provides the use of a compound formula (I) wherein R.sup.1 and R.sup.2 independently represent H or C.sub.1-C.sub.6 alkyl, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of: dermatological disorders; peripheral neuropathies; arthritis; gastrointestinal or urogenital disease; **headache** associated with substances or their withdrawal; tension **headache**; pediatric migraine; post-traumatic dysautonomic cephalgia; orofacial pain; allergic or chronic obstructive airways diseases, glaucoma or ocular inflammation; or prophylaxis of migraine 1

Excerpt(s): This invention relates to new uses of certain indole derivatives in the treatment or prophylaxis of medical disorders. International Patent Application WO 92/06973 discloses a series of indole derivatives which are potent serotonin (5-HT) agonists. These compounds are useful for treating disorders arising from deficient serotonergic neurotransmission comprising hypertension, depression, anxiety, eating disorders, obesity, drug abuse, cluster **headache**, migraine, pain and chronic paroxysmal hemicrania and **headache** associated with vascular disorders. The compounds covered by WO 92/06973 include (R)-5-(methylaminosulphonylmethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-i- ndole (Example 5A, known as CP-122,288) and (R)-5-(methylaminosulphonylmet- hyl)-3-(pyrrolidin-2-ylmethyl)-1H-indole (Example 6A, known as CP-122,638). It is known that CP-122,288 and CP-122,638 exhibit potency against neurogenic inflammation in dura mater [W. S. Lee and M. A. Moskowitz, Brain Research, 626 (1993), 303-305].

# • Methods and compositions for treating headache pain with topical NSAID compositions

Inventor(s): Caldwell, Larry; (San Jose, CA), Galer, Bradley S.; (West Chester, PA)

Correspondence: Bozicevic, Field & Francis Llp; 200 Middlefield RD; Suite 200; Menlo Park; CA; 94025; US

Patent Application Number: 20030119892

Date filed: December 26, 2001

Abstract: Methods and compositions are provided for treating a host suffering from **headache** pain. In the subject methods, a topical NSAID formulation is applied to a keratinized skin site proximal to the pain associated with the **headache** pain, e.g., a keratinized skin surface of the head, such as the forehead, temple, etc. Practice of the subject methods results in at least a reduction in the intensity of the pain associated with the **headache**. The subject methods and compositions find use in the treatment of a variety of **headache** conditions.

Excerpt(s): The field of this invention is the treatment of **headache** pain. Headaches are a common problem affecting a large segment of the population. **Headaches**, such as tension type and migraine **headaches**, occur both intermittently and chronically, and can arise in response to variety of stimulants, including stress, injury, toxins in the environment and the like. A variety of therapeutic agents have been developed for use in the treatment of patients suffering from **headache** pain. Some agents, such as aspirin, acetaminophen, vasoconstrictors and NSAIDs, e.g. ibuprofen and naprosyn, are administered systemically. Despite the prevalence of this form of treatment for **headache** pain, in some cases, systemic administration is not recommended. For example, oral administration of aspirin can result in stomach upset and patient discomfort. Furthermore, the agent can exert host systemic toxicity which may outweigh any therapeutic benefits provided by the agent. Finally, since the agent is administered systemically, its effects are also systemic, which may not be desired.

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

# • Methods for the treatment of primary headache disorders using prostanoid EP4 receptor antagonists, and assays for agents for such treatment

Inventor(s): Baxter, Gordon S.; (Hertfordshire, GB), Coleman, Robert A.; (Hertfordshire, GB), Tilford, Nicholas; (Hertfordshire, GB)

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Patent Application Number: 20030158240

Date filed: February 19, 2003

Abstract: The present invention provides for the treatment of primary **headache** disorders, particularly migraine, using antagonists of the EP.sub.4 receptor for prostaglandin E2. Particular EP.sub.4 receptor antagonists include azole compounds of formula (I): 1wherein R.sup.1 is a group such as lower alkyl substituted with carboxy; R.sup.2 is hydrogen or lower alkyl, R.sup.3 and R.sup.4 are aryl optionally substituted with halogen, 2in which --A.sup.1-- is a single bond or lower alkylene, 3is a cyclo group,--A.sup.3-- is a single bond or lower alkylene, and X is O, NH or S;or a salt or its solvate thereof.

Excerpt(s): This application is a continuation-in-part of PCT/GB98/02895, filed Sep. 25, 1998, which designated the U.S., which on filing claimed benefit of GB 9720270.9, filed Sep. 25, 1997, the entire contents of each of which are hereby incorporated by reference. The present invention relates to a method of treatment of primary **headache** disorders and drug-induced **headaches** in humans and other mammals and to the use of compounds in the preparation of a medicament for the treatment of primary **headache** disorders and drug-induced **headaches**. There is a widely held view that the pain of migraine **headache** originates from abnormally distended blood vessels in the cerebral vasculature. Dilatation in cerebral blood vessels, would cause local pressure resulting in the activation of local sensory pathways and pain. This can be the case also for the other aforementioned primary **headache** disorders and certain drug-induced **headaches**.

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

# Methods for treating disorders using norastemizole in combination with other active ingredients

Inventor(s): Aberg, A. K. Gunnar; (Westborough, MA), Woosley, Raymond L.; (Washington, DC)

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Patent Application Number: 20020137768

Date filed: March 28, 2002

Abstract: Methods and compositions are disclosed utilizing metabolic derivatives of astemizole for the treatment of allergic disorders while avoiding the concomitant liability of adverse effects associated with the astemizole. The metabolic derivatives of astemizole are also useful for the treatment of retinopathy and other small vessel disorders associated with diabetes mellitus and such other conditions as may be related to the antihistamine activity of astemizole. For example, the metabolic derivatives of astemizole are useful for the treatment of asthma, motion sickness, and vertigo, without the concomitant liability of adverse effects associated with astemizole. Furthermore, the metabolic derivatives of astemizole, in combination with non-steroidal anti-inflammatory agents or other non-narcotic analgesics, or in combination with a decongestant, cough suppressant/antitussive or expectorant, are useful for the treatment of cough, cold, cold-like, and/or flu symptoms and the discomfort, headache, pain, fever, and general malaise associated therewith, without the concomitant liability of adverse effects associated therewith without the concomitant liability of adverse effects associated therewith astemizole.

Excerpt(s): This invention relates to novel pharmaceutical compositions containing desmethylastemizole, 6-hydroxydesmethylastemizole and norastemizole. These compositions possess potent antihistaminic activity and are useful in treating allergic rhinitis, asthma and other allergic disorders while avoiding adverse effects associated with the administration of other antihistamines, such as astemizole, including but not limited to cardiac arrhythmias, drowsiness, nausea, fatigue, weakness and headache. Also, these compositions, in combination with non-steroidal anti-inflammatory agents or other non-narcotic analgesics, are useful for the treatment of cough, cold, cold-like, and/or flu symptoms and the discomfort, headache, pain, fever, and general malaise associated therewith. The aforementioned combinations may optionally include one or more other active components including а decongestant, cough suppressant/antitussive, or expectorant. Additionally, these novel pharmaceutical compositions containing desmethylastemizole, 6-hydroxydesmethylastemizole and norastemizole are useful in treating motion sickness, vertigo, diabetic retinopathy, small vessel complications due to diabetes and such other conditions as may be related to the activity of these s derivatives as antagonists of the H-1 histamine receptor while avoiding the adverse effects associated with the administration of other antihistamines, such as astemizole. Also disclosed are methods for treating the above-described conditions in a human while avoiding the adverse effects that are associated with the administration of other antihistamines, such as astemizole, by administering the aforementioned pharmaceutical compositions containing desmethylastemizole, 6-hydroxydesmethylastemizole and norastemizole to said human.

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

# • Methods for treating indomethacin responsive headaches

Inventor(s): Galer, Bradley S.; (West Chester, PA), Newman, Lawrence; (Goldens Bridge, NY)

Correspondence: Bret E. Field; Bozicevic, Field & Francis Llp; Suite 200; 200 Middlefield Road; Menlo Park; CA; 94025; US

Patent Application Number: 20020143047

Date filed: January 5, 2001

Abstract: Methods and compositions, e.g., kits, are provided for treating a host suffering from an indomethacin responsive **headache** syndrome. In the subject methods, a topical indomethacin formulation is applied to a keratinized skin site proximal to the pain associated with the **headache** syndrome, e.g. a keratinized skin surface of the head, such as the forehead, temple, etc. Practice of the subject methods results in at least a reduction in the intensity of the pain associated with the syndrome. The subject methods and compositions find use in the treatment of a variety of indomethacin responsive **headache** syndromes that are absolutely responsive to indomethacin therapy and syndromes that are variably responsive to indomethacin therapy.

Excerpt(s): The technical field of the invention is indomethacin-responsive **headaches** and the treatment thereof. The indomethacin-responsive **headaches** are a group of uncommon primary **headache** disorders that, by accepted definition of the International **Headache** Society Diagnostic Criteria, only demonstrate a prompt remission following therapy with indomethacin. The indomethacin responsive **headaches** can be further separated into two subcategories, based upon clinical features and degree of responsiveness to indomethacin. Those syndromes that exhibit an absolute response to therapy include the paroxysmal hemicranias and hemicrania continua. Syndromes exhibiting a variable response to therapy include idiopathic stabbing **headaches** (also called ice-pick headaches), and the benign forms of cough **headache**, exertional **headache**, and **headaches** associated with sexual activity. Unlike other primary **headache** disorders such as migraine, tension-type and cluster **headaches**, the indomethacin responsive **headache** conditions are resistant to treatment with all other classes of therapeutic agents.

#### • Methods for treating migraine headaches

Inventor(s): Saathoff, Myra K.; (Houston, TX)

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Patent Application Number: 20020156508

Date filed: April 18, 2001

Abstract: The present invention generally relates to various systems and methods for the treatment of a migraine **headache** and related malady(s) through the filtering a portion of ambient light transmitted to the eye of a patient.

Excerpt(s): The present invention generally relates to methods and apparatuses for treating migraine headaches and related maladies. An embodiment of the method generally comprises the filtering of a portion of ambient light transmitted into the eye of a patient. Migraine headaches are a very common disorder that afflicts numerous people on a regular basis. A migraine **headache** has been defined in the art, generally, as an episodic headache lasting a finite time, in the range of a small amount of time to days. The small amount of time could be minutes to a few hours. These episodic headaches are often, but not always, associated with an aura followed by gastrointestinal discomfort, dizziness, pulsatile pain, increased pain through normal physical activity, photophobia, phonophobia and/or visual disturbances. It is common that the discomfort and disturbance is of such a nature and frequencies so as to adversely affect the afflicted individual's lifestyle. As used herein, the following terms mean and refer to the definitions given. The term "patient" means and refers to an individual afflicted with a migraine headache. The term "migraine headache" means and refers to an episodic headaches are often, but not always, associated with gastrointestinal discomfort, dizziness, pulsatile pain, increased pain through normal physical activity, photophobia, phonophobia and/or visual disturbances. The term "maladies" or "malady" means and refers to premenstrual syndrome, stress, and other related types of maladies, including migraine headaches. The term "filter" or "filtering" means and refers to filtering, interfering, shading, at least partially blocking and the like.

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

### • Methods for treating tension headache

Inventor(s): Aoki, K. Roger; (Laguna Hill, CA), Carlson, Steven R.; (Laguna Niguel, CA), Grayston, Michael W.; (Irvine, CA), Leon, Judith M.; (Laguna Niguel, CA)

Correspondence: Stephen Donovan; Allergan, INC.; 2525 Dupont Drive, T2-7h; Irvine; CA; 92612; US

Patent Application Number: 20020197279

Date filed: July 29, 2002

Abstract: A method and composition for treating a patient suffering from a disease, disorder or condition and associated pain include the administration to the patient of a therapeutically effective amount of a neurotoxin selected from a group consisting of Botulinum toxin types A, B, C, D, E, F and G.

Excerpt(s): The present invention provides novel methods for treating various disorders and conditions, with Botulinum toxins. Importantly, the present invention provides methods useful in relieving pain related to muscle activity or contracture and therefore

is of advantage in the treatment of, for example, muscle spasm such as Temporomandibular Joint Disease, low back pain, myofascial pain, pain related to spasticity and dystonia, as well as sports injuries, and pain related to contractures in arthritis. Heretofore, Botulinum toxins, in particular Botulinum toxin type A, has been used in the treatment of a number of neuromuscular disorders and conditions involving muscular spasm; for example, strabismus, blepharospasm, spasmodic torticollis (cervical dystonia), oromandibular dystonia and spasmodic dysphonia (laryngeal dystonia). The toxin binds rapidly and strongly to presynaptic cholinergic nerve terminals and inhibits the exocytosis of acetylcholine by decreasing the frequency of acetylcholine release. This results in local paralysis and hence relaxation of the muscle afflicted by spasm. For one example of treating neuromuscular disorders, see U.S. Pat. No. 5,053,005 to Borodic, which suggests treating curvature of the juvenile spine, i.e., scoliosis, with an acetylcholine release inhibitor, preferably Botulinum toxin A.

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

# • Modulators of KCNQ potassium channels and use thereof in treating migraine and mechanistically related diseases

Inventor(s): Dworetzky, Steven I.; (Middlefield, CT), Gribkoff, Valentin K.; (Wallingford, CT), Hewawasam, Piyasena; (Middletown, CT), Kinney, Gene G.; (Collegeville, PA)

Correspondence: Stephen B. Davis; Bristol-myers Squibb Company; Patent Department; P. O. Box 4000; Princeton; NJ; 08543-4000; US

Patent Application Number: 20020128277

Date filed: February 14, 2002

Abstract: Compounds which function as modulators, particularly, openers, of human KCNQ potassium channel proteins or polypeptides, particularly, central nervous system (CNS)-located KCNQ potassium channels, and heteromultimers thereof, and their use in the treatment of migraine are provided by the present invention. One novel type of potassium channel polypeptide openers provided by the present invention is the fluorooxindole compounds, described for the first time as therapeutics for the treatment of migraine by preventing the asynchronous firing of neurons. Other KCNQ potassium channel opener compounds that are also useful in the treatments of the invention include 2,4-disubstituted pyrimidine-5-carboxamide derivatives. One or more of the compounds according to the present invention may be utilized alone, in combination, or in conjunction with other treatment modalities for reducing, ameliorating and/or alleviating migraine or diseases similar to, or mechanistically related to, migraine, e.g., cluster **headache**.

Excerpt(s): This is a non-provisional application which claims the benefit of U.S. Provisional Application No. 60/269,967 filed Feb. 20, 2001. The present invention relates generally to the KCNQ family of potassium channels and their involvement in the treatment of migraine and associated disorders. More specifically, the present invention provides modulators of central nervous system (CNS)-related potassium channel polypeptides, e.g., KCNQ2, KCNQ3, KCNQ4, KCNQ5, or heteromultimers thereof, particularly human CNS KCNQ potassium channels, which are effective in reducing, ameliorating and treating migraine (also termed migraine headache). Preferably, the KCNQ potassium channel polypeptides and are useful in the treatment of neurological and neurophysiological conditions, disorders and diseases, with particular regard to migraine. Potassium (K.sup.+) channels are membrane-spanning

proteins that generally act to hyperpolarize neurons. Physiological studies indicate that potassium currents are found in most cells and are associated with a wide range of functions, including the regulation of the electrical properties of excitable cells. Depending on the type of potassium channel, its functional activity can be controlled by transmembrane voltage, different ligands, protein phosphorylation, or other second messengers.

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

Morinda citrifolia enhanced naturaceutical formulation and method for treating and preventing migraine headaches

Inventor(s): Jensen, Claude Jarakae; (Cedar Hills, UT), Palu, Afa Kehaati; (Orem, UT), Story, Stephen; (Alpine, UT)

Correspondence: Kirton & Mcconkie; 1800 Eagle Gate Tower; 60 East South Temple; Salt Lake City; UT; 84111; US

Patent Application Number: 20030108630

Date filed: October 31, 2002

Abstract: The present invention features methods and formulations or compositions, such as a naturaceutical formulation, for treating and preventing **headaches**, and particularly migraine **headaches**, as well as methods and formulations for treating the conditions and symptoms often associated with migraine **headaches**. The naturaceutical formulations comprise an identified amount of a processed Morinda citrifolia product by weight, and the method comprises the prophylactic administration of the processed Morinda citrifolia product-based naturaceutical formulation in a safe, pre-determined or identified amount for a safe, pre-determined frequency, for a safe, pre-determined duration of time.

Excerpt(s): The present invention relates to methods and naturaceutical formulations and substances for treating and preventing headaches, and particularly migraine headaches, and their associated symptoms and conditions. Specifically, the present invention relates to Morinda citrifolia-based methods and formulations for treating and relieving pre-existing headaches, as well as to methods and formulations for preventing the onset or reducing the onset potential of additional, future headaches. The present invention is particularly suited for treatment and prevention of migraine headaches as commonly experienced in mammals, and particularly humans. The lifetime prevalence of migraine headaches is consistent around the world ranging from 6% to 12% in men and 15% to 25% in women. The maximum prevalence occurs between the ages of 30 and 50 in both men and women and can persist through the age of 70 to 80. Very often migraine headaches are responsive to standard medical intervention, but not always. As many as 73% of patients have frequent low-grade headaches between attacks and these are increasingly recognized as having migraine origin as well. The costs in terms of human suffering and economic losses are large: an average of \$817 is spent in the United States per year on direct treatment. Approximately 270 working days per year are lost through inability to work for every 1000 migraine sufferers in the work force. In addition, migraine headaches are now recognized to contribute to a number of comorbid disorders over life including panic disorder, anxiety disorder and affective disorders in the younger, and hypertension, myocardial infarction and stroke in the older patient populations. While medications can be effective, their overuse is also attributed to be the cause of drug-induced refractory headaches. Some patients seeking relief will turn to alternative therapies such as chiropractic, acupuncture and naturaceuticals (herbs, vitamin and other natural food supplements). As with every disease, the earlier they can be identified, the earlier their cause can be determined. Early detection results in treatment. Unlike other diseases however, migraine **headaches** do not seem to follow this general deduction as there exists several factors or conditions that can trigger a migraine **headache** or the symptoms of a migraine **headache**.

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

## • Nitroglycerin-menthol potentiation for treatment of angina

Inventor(s): Busiashvili, Yuri; (Pacific Palisades, CA)

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Patent Application Number: 20020193435

Date filed: March 21, 2002

Abstract: The strength of a nitroglycerin dosage to be administered to patients suffering from angina can be reduced when a portion of the dosage is replaced with menthol containing substances (MCS). MCS and specifically 1% Menthol has been found to potentate the effect of nitroglycerin. Accordingly, MCS can be used as a substitute for a portion of the nitroglycerin dosage administered to a patient. Side-effects common to nitroglycerin usage such as **headache** and fainting are significantly reduced when a nitroglycerin/MCS solution is used which has 50% of the nitroglycerin dosage per spray commonly used without sacrificing treatment effectiveness.

Excerpt(s): This application claims the priority of U.S. Provisional Application bearing serial No. 60/279,154 filed on Mar. 27, 2001. This invention pertains to cardiac medication and specifically to the treatment of angina with a mixture of nitroglycerin (NTG) and menthol containing substances (MCS). Nitroglycerin spray is widely used in patients with coronary artery disease and angina.

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

# Pharmaceutical composition and method of modulating cholinergic function in a mammal

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Patent Application Number: 20030008892

Date filed: March 25, 2002

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Abstract: A pharmaceutical composition and method of modulating cholinergic function in a mammal comprising administration of a NRPA compound or a pharmaceutically acceptable salt thereof; and an anti-emetic/anti-nausea agent or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier. The NRPA compound and the anti-emetic/anti-nausea agent are present in amounts that render the composition effective modulating cholinergic function or in the treatment of a diorder or condition selected from inflammatory bowel disease (including but not limited to ulcerative colitis, pyoderma gangrenosum and Crohn's disease), irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supranuclear palsy, chemical dependencies and addictions (e.g., dependencies on, or addictions to nicotine (and/or tobacco products), alcohol, benzodiazepines, barbiturates, opioids or cocaine), **headache**, migraine, stroke, traumatic brain injury (TBI), obsessive-compulsive disorder (OCD), psychosis, Huntington's chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multiinfarct dementia, age-related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome. The method of using these compositions is also disclosed.

Excerpt(s): The present invention relates to pharmaceutical compositions for modulating cholinergic function in a mammal comprising a nicotinic receptor partial agonist compound in combination with an anti-emetic/anti-nausea agent and a pharmaceutically acceptable carrier. The nicotinic receptor partial agonists (NRPAs) included herein are aryl fused azapolycyclic compounds. NRPAs are not limited to those described here. The term NRPA refers to all chemical compounds which bind at neuronal nicotinic acetylcholine specific receptor sites in mammalian tissue and elicit a partial agonist response. A partial agonist response is defined here to mean a partial, or incomplete functional effect in a given functional assay. Additionally, a partial agonist will also exhibit some degree of antagonist activity by its ability to block the action of a full agonist (Feldman, R. S., Meyer, J. S. & Quenzer, L. F. Principles of Neuropsychopharmacology, 1997; Sinauer Assoc. Inc.). The present invention may be used to treat mammals (e.g. humans) for inflammatory bowel disease (including but not limited to ulcerative colitis, pyoderma gangrenosum and Crohn's disease), irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supranuclear palsy, chemical dependencies and addictions (e.g., dependencies on, or addictions to nicotine (and/or tobacco products), alcohol, benzodiazepines, barbiturates, opioids or cocaine), headache, migraine, stroke, traumatic brain injury (TBI), obsessive-compulsive disorder (OCD), psychosis, Huntington's chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multiinfarct dementia, age-related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome with a decrease in the incidence and severity of unwanted side effects such as nausea and/or stomach upset. The present invention also relates to the combination use of NRPAs and anti-emetic/anti-nausea agents resulting in modulation of cholinergic function without nausea. The combination will provide an improved treatment paradigm than NRPAs alone.

### • Pharmaceutical kit for migraine headache treatment

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Patent Application Number: 20030196929

Date filed: April 19, 2002

Abstract: A pharmaceutical kit for treating migraine **headaches** and method of preparing the kit that includes a therapeutically effective dosage of pharmaceutical compounds used in the treatment of migraine **headache**. The pharmaceutical kit is manufactured with a predetermined number of dosage units of migraine treating pharmaceutical compounds. Additionally the kit provides all components necessary for the administering of the drugs in a safe and convenient manner. An aspect of the pharmaceutical kit may include injections and nasal sprays that are fast acting for relief of the migraine sufferer. A preferred pharmaceutical kit with only oral dosage units of drugs may be provided as an attachment to a water bottle.

Excerpt(s): The present invention broadly relates to a pharmaceutical kit and method of packaging the kit for treating migraine **headaches**. Migraine is an age old disease which has been described and dealt with in various ways throughout history by many cultures and civilization. For example, old English literature described migraine as "Hemicrania", implying that migraine **headache** is unilateral in the head. However migraine does not always attack in a unilateral manner. It took several centuries to understand the scientific basis and recognize the wide clinical spectrum of this very common illness. As of recent times, in the United States alone, there are 28 million people suffering from migraine. Of that population, approximately 21 million are female and 7 million are male. One in four households has at least one migraine sufferer. Migraine prevalence peaks in the 25 to 55 year age ranges in both genders. In the 1999 HIS (International Headache Society) estimate, 52% of the total population of migraine cases remain undiagnosed. The undiagnosed sufferers are most likely self-medicating with over the counter medications. "Migraine Awareness", i.e., public knowledge of migraine illness, is much more prevalent in the urban areas than in the interior heartland of the United States, for example.

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

## • Piperidine derivatives as subtype selective N-methyl-D-aspartate antagonists

Inventor(s): Kornberg, Brian Edward; (Ann Arbor, MI), Lewthwaite, Russell Andrew; (Cambridge, GB), Manning, David; (Duanesburg, NY), Nikam, Sham Shridhar; (Ann Arbor, MI), Scott, Ian Leslie; (Delanson, NY)

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Patent Application Number: 20030018021

Date filed: November 30, 2001

Abstract: Described are piperidines of Formula I 1and pharmaceutically acceptable salts thereof. The compounds of Formula I are antagonists of NMDA receptor channel complexes useful for treating cerebral vascular disorders such as, for example, stroke, cerebral ischemia, central nervous system disorders, depression, trauma, hypoglycemia,

neurodegenerative disorders, anxiety, migraine **headache**, convulsions, Parkinson's disease, aminoglycoside antibiotics-induced hearing loss, psychosis, glaucoma, CMV retinitis, opioid tolerance or withdrawal, pain, especially chronic pain, neuropathic pain, or surgical pain, or urinary incontinence.

Excerpt(s): The invention relates to piperidine derivatives as N-Methyl-D-Aspartate (NMDA) antagonists useful in the treatment of diseases and disorders responsive to antagonism of NMDA receptors. Many of the physiological and pathophysiological effects of the endogenous excitatory neurotransmitter glutamate are mediated via actions at N-Methyl-D-Asparate (NMDA) receptors. Over-excitation of the NMDA receptors on postsynaptic cells-mediated by excessive release of glutamate from nerve endings or glial cells-results in a massive calcium ion influx through a calcium ion channel into neuronal cells, leading to neuronal cell death. These events occur under ischemic or hypoxic conditions such as, for example, stroke, hypoglycemia, cardiac arrest, or acute physical trauma. NMDA receptors in vivo form an NMDA receptor channel complex in cell walls comprising at least three binding domains, including a glutamic acid (or NMDA) recognition site, a channel blocking binding site, and a strychnine-insensitive glycine binding site. Physiologically, a blockade of at least one of these sites terminates the channel opening of the NMDA receptor, thereby preventing calcium ion influx into cells. Accordingly, an NMDA receptor antagonist is therapeutically useful because it minimizes damage to the central nervous system induced by calcium ion influx under ischemic or hypoxic conditions.

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### • Pressure clamp for relieving a headache

Inventor(s): Curtis, Patrick M.; (St. Petersburg, FL)

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Patent Application Number: 20030195558

Date filed: May 15, 2003

Abstract: A clamp is positioned in a fleshy area of a person's hand between the thumb and index figure. The clamp has a top and bottom arm with a thumb screw to close a gap between the arms over the fleshy area of a person's hand and is left in place for two to three minutes or until the person's **headache** is relieved. Thereafter, the clamp is removed and stored for future use.

Excerpt(s): This application is a continuation-in-part from application Ser. No. 09/344,019, filed Jun. 25, 1999. and a divisional of application Ser. No. 09/694,454, filed Oct. 23, 2000. This invention relates to a device for relieving **headaches**. More particularly, it relates to a device and method for relieving a **headache** wherein there is provided a device for clamping to the hand of a person experiencing a **headache** to effect a reduction of tension. Clamping devices are well known in the prior art. Numerous designs of clamps have been used for years everywhere from carpentry to manufacturing to medical uses. For instance, clamps are used extensively by carpenters when gluing two structures together; in manufacturing environments by tool and die makers; and by doctors in surgical procedures (i.e., to "clamp-off" arteries).

## • Regulation of human substance p-like g protein-coupled receptor

Inventor(s): Ramakrishnan, Shyam; (Brighton, MA)

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Patent Application Number: 20030104435

Date filed: September 11, 2002

Abstract: Reagents which regulate human substance P G protein-coupled receptor (SP-GPCR) protein and reagents which bind to human SP-GPCR gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, urinary incontinence, inflammatory diseases (e.g., arthritis, psoriasis, asthma and inflammatory bowel disease), anxiety, depression or dysthymic disorders, cluster **headache**, colitis, psychosis, pain, allergies such as eczema and rhinitis, chronic obstructive airways disease, hypersensitivity disorders such as poison ivy, vasospastic diseases such as angina, migraine and Reynaud's disease, fibrosing and collagen diseases such as scleroderma and eosinophilic fascioliasis, reflex sympathetic dystrophy such as shoulder/hand syndrome, addiction disorders such as alcoholism, stress related somatic disorders, peripheral neuropathy, neuralgia, neuropathological disorders such as Alzheimer's disease, AIDS related dementia, diabetic neuropathy and multiple sclerosis, disorders related to immune enhancement or suppression such as systemic lupus erythematosus, and rheumatic diseases such as fibrositis.

Excerpt(s): The invention relates to the area of G-protein coupled receptors. More particularly, it relates to the area of human substance P-like G protein-coupled receptor and its regulation. Many medically significant biological processes are mediated by signal transduction pathways that involve G-proteins (Lefkowitz, Nature 351, 353-354, 1991). The family of G-protein coupled receptors (GPCR) includes receptors for hormones, neurotransmitters, growth factors, and viruses. Specific examples of GPCRs include receptors for such diverse agents as dopamine, calcitonin, adrenergic hormones, endothelin, cAMP, adenosine, acetylcholine, serotonin, histamine, thrombin, kinin, follicle stimulating hormone, opsins, endothelial differentiation gene-1, rhodopsins, odorants, cytomegalovirus, G-proteins themselves, effector proteins such as phospholipase C, adenyl cyclase, and phosphodiesterase, and actuator proteins such as protein kinase A and protein kinase C. GPCRs possess seven conserved membranespanning domains connecting at least eight divergent hydrophilic loops. GPCRs (also known as 7TM receptors) have been characterized as including these seven conserved hydrophobic stretches of about 20 to 30 amino acids, connecting at least eight divergent hydrophilic loops. Most GPCRs have single conserved cysteine residues in each of the first two extracellular loops, which form disulfide bonds that are believed to stabilize functional protein structure. The seven transmembrane regions are designated as TM1, TM2, TM3, TM4, TM5, TM6, and TM7. TM3 has been implicated in signal transduction.

#### Subtype-selective NMDA receptor ligands and the use thereof

Inventor(s): Araldi, Gian Luca; (Washington, DC), Bigge, Christopher F.; (Ann Arbor, MI), Cai, Sui Xiong; (Foothill, CA), Guzikowski, Anthony P.; (Eugene, OR), Keana, John F.W.; (Eugene, OR), Lamunyon, Donald; (Junction City, OR), Lan, Nancy C.; (South Pasadena, CA), Zhou, Zhang-Lin; (Irvine, CA)

Correspondence: Fitzpatrick Cella Harper & Scinto; 30 Rockefeller Plaza; New York; NY; 10112; US

Patent Application Number: 20030144319

Date filed: November 14, 2002

Abstract: The invention relates to subtype-selective NMDA receptor ligands and the use thereof for treating or preventing neuronal loss associated with stroke, ischemia, CNS trauma, hypoglycemia and surgery, as well as treating neurodegenerative diseases including Alzheimer's disease, amyotrophic lateral sclerosis, Huntington's disease and Down's syndrome, treating or preventing the adverse consequences of the overstimulation of the excitatory amino acids, treating anxiety, psychosis, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine **headache**, chronic pain, Parkinson's disease, glaucoma, CMV retinitis, urinary incontinence, opioid tolerance or withdrawal, and inducing anesthesia, as well as for enhancing cognition.

Excerpt(s): This invention is related to 2-substituted piperidine analogs. The analogs are selectively active as antagonists of N-methyl-D-aspartate (NMDA) receptor subtypes. The invention is also directed to the use of 2-substituted piperidine analogs as neuroprotective agents for treating conditions such as stroke, cerebral ischemia, central nervous system trauma, hypoglycemia, anxiety, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine headaches, chronic pain, glaucoma, CMV retinitis, psychosis, urinary incontinence, opioid tolerance or withdrawal, or neurodegenerative disorders such as lathyrism, Alzheimer's Disease, Parkinsonism and Huntington's Disease. Excessive excitation by neurotransmitters can cause the degeneration and death of neurons. It is believed that this degeneration is in part mediated by the excitotoxic actions of the excitatory amino acids (EAA) glutamate and aspartate at the N-methyl-D-Aspartate (NMDA) receptor. This excitotoxic action is considered responsible for the loss of neurons in cerebrovascular disorders such as cerebral ischemia or cerebral infarction resulting from a range of conditions, such as thromboembolic or hemorrhagic stroke, cerebral vasospasms, hypoglycemia, cardiac arrest, status epilepticus, perinatal asphyxia, anoxia such as from drowning, pulmonary surgery and cerebral trauma, as well as lathyrism, Alzheimer's Disease, Parkinson's Disease and Huntington's Disease. Excitatory amino acid receptor antagonists that block NMDA receptors are recognized for usefulness in the treatment of disorders. NMDA receptors are intimately involved in the phenomenon of excitotoxicity, which may be a critical determinant of outcome of several neurological disorders. Disorders known to be responsive to blockade of the NMDA receptor include acute cerebral ischemia (stroke or cerebral trauma, for example), muscular spasm, convulsive disorders, neuropathic pain and anxiety, and may be a significant causal factor in chronic neurodegenerative disorders such as Parkinson's disease [T. Klockgether, L. Turski, Ann. Neurol. 34, 585-593 (1993)], human immunodeficiency virus (HIV) related neuronal injury, amyotrophic lateral sclerosis (ALS), Alzheimer's disease [P. T. Francis, N. R. Sims, A. W. Procter, D. M. Bowen, J. Neurochem. 60 (5), 1589-1604 (1993)] and Huntington's disease. [See S. Lipton, TINS 16 (12), 527-532 (1993); S. A. Lipton, P. A. Rosenberg, New Eng. J. Med. 330 (9), 613-622 (1994); and C. F. Bigge, Biochem. Pharmacol. 45, 1547-1561 (1993) and references cited therein.]. NMDA receptor antagonists may also be used to prevent tolerance to opiate analgesia or to help control withdrawal symptoms from addictive drugs (Eur. Pat. Appl. 488,959A).

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

### • Topiramate salts and compositions comprising them

Inventor(s): Almarsson, Orn; (Shrewsbury, MA), Peterson, Matthew L.; (Framingham, MA), Remenar, Julius; (Framingham, MA)

Correspondence: Saliwanchik Lloyd & Saliwanchik; A Professional Association; 2421 N.W. 41st Street; Suite A-1; Gainesville; FL; 326066669

Patent Application Number: 20030166581

Date filed: November 18, 2002

Abstract: The invention encompasses novel salts of topiramate, and pharmaceutically acceptable polymorphs, solvates, hydrates, dehydrates, co-crystals, anhydrous, or amorphous forms thereof, as well as pharmaceutical compositions and pharmaceutical unit dosage forms containing the same. In particular, the invention encompasses pharmaceutically acceptable salts of topiramate, including without limitation topiramate sodium, topiramate lithium, topiramate potassium, or polymorphs, solvates, hydrates, dehydrates, co-crystals, anhydrous, and amorphous forms thereof. The invention further encompasses novel co-crystals or complexes of topiramate, as well as pharmaceutical compositions comprising them. The invention also encompasses methods of treating or preventing a variety of diseases and conditions including, but not limited to, seizures, epileptic conditions, tremors, cerebral function disorders, obesity, neuropathic pain, affective disorders, tobacco cessation, migraines, and cluster **headache.** 

Excerpt(s): This application is related to U.S. provisional patent application Nos. 60/356,764, filed Feb. 15, 2002, 60/380,288, filed May 15, 2002, and \_\_\_\_\_\_ filed Aug. 30, 2002, all of which are incorporated herein by reference in their entireties. This invention relates to compounds, pharmaceutical compositions, and methods for the treatment or prevention of seizures, epilepsy, tremors, affective disorders, obesity, neuropathic pain, and migraines. Topiramate is a white crystalline powder with a solubility in water of 9.8 mg/mL, and it is freely soluble in acetone, chloroform, dimethylsulfoxide, and ethanol. See, Physician's Desk Reference, 56.sup.th ed., pp. 2590-2595 (2002).

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

## • Transdermal migraine therapy

Inventor(s): Aung-Din, Ronald; (Sarasota, FL)

Correspondence: Davidson, Davidson & Kappel, Llc; 485 Seventh Avenue, 14th Floor; New York; NY; 10018; US

Patent Application Number: 20030013753

Date filed: June 5, 2002

Abstract: The invention is directed to formulations and methods of treating a migraine and/or cluster **headache** with a serotonin agonist, pharmaceutically acceptable salt thereof, or derivative thereof.

Excerpt(s): The present application claims priority from U.S. Provisional Application No. 60/296,286, filed Jun. 5, 2001, the disclosure of which is hereby incorporated by reference in its entirety. Migraine headaches are a debilitating condition in which some 53 million persons per year suffer acute pain. Frequently, migraine is accompanied by sickness and vomiting and a sensitivity to light and noise. Since the discovery of serotonin (5-hydroxytryptamine, 5-HT) over four decades ago, the cumulative results of many diverse studies have indicated that serotonin plays a significant role in the functioning of the mammalian body, both in the central nervous system and in peripheral systems as well. Morphological studies of the central nervous system have shown that serotonergic neurons, which originate in the brain stem, form a very diffuse system that projects to most areas of the brain and spinal cord. R. A. O'Brien, Serotonin in Mental Abnormalities, 1: 41 (1978); H. W. M. Steinbusch, HANDBOOK OF CHEMICAL NEUROANATOMY, Volume 3, Part II, 68 (1984); N. E. Anden, et al., Acta Physiologica Scandinavia, 67: 313 (1966). These studies have been complemented by biochemical evidence that indicates large concentrations of 5-HT exist in the brain and spinal cord. H. W. M. Steinbusch, supra.

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

### • Treatment of migraine headache

Inventor(s): Chowhan, Zakauddin T.; (Gaithersburg, MD), Plachetka, John R.; (Chapel Hill, NC)

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Patent Application Number: 20030040537

Date filed: September 26, 2002

Abstract: The invention is directed to pharmaceutical compositions useful in the treatment of migraine. The compositions contain metoclopramide and one or more NSAIDs in unit dosage form. By selecting NSAIDs that are non-acidic or segregating the metoclopramide and NSAID, the storage life of the compositions has been increased. Also disclosed are coordinated dosage forms for the sequential release of drugs. The invention encompasses methods of treating migraine using any of these dosage forms.

Excerpt(s): This application is a continuation-in-part of U.S. Ser. No. 08/966,506, filed Nov. 10, 1997, which is a continuation-in-part of U.S. application Ser. No. 08/748,332, filed Nov. 12, 1996. The present invention is directed to compositions comprising metoclopramide and a second drug, particularly an analgesic. These compositions may be used as a treatment for migraine and other disorders. Migraine is a painful syndrome characterized by unilateral, pulsating headaches, nausea, vomiting, and sensitivity to light and sound. Approximately 23 million Americans presently suffer from this disorder. Drugs that have been used in an attempt to treat migraine include: ergotamine and ergotamine-like agents; serotonin agonists; and caffeine with ergots or other pharmacologic agents (see e.g., Silberstein, S. D., Curr. Opinion Neurology 7:258-263 (1994); Welch, K. M. A., New Engl J. Med. 329:1476-1483 (1993); Kumar, K. L., J. Gen. Int. Med. 9:339-348 (1994); Saadah, H., Headache 32:95-97 (1992); and Becker, Arzneimittelforshung 42(4):552-555 (1992)). All of these drugs are thought to initially relieve migraine-associated pain by causing vasoconstriction. Unfortunately, this leads to numerous side effects such as chest pain or pressure, flushing, generalized tingling sensations, nausea, vomiting, pain in the legs and arms, asthenia, drowsiness, and dizziness. Acute ergotism is a particularly pernicious side effect of ergot drugs and is characterized by severe central and peripheral vasoconstriction, nausea, vomiting, diarrhea, colic, **headache**, vertigo, paresthesia, and possibly convulsive seizures.

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

### • Use of a vitamin combination for the treatment of primary headaches

Inventor(s): Valletta, Giampiero; (Ceprano, IT)

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Patent Application Number: 20030181459

Date filed: February 5, 2003

Abstract: Use of a combination of two vitamin compounds, i.e. riboflavin (also known as vitamin B.sub.2) and nicotinic acid (also referred to as niacin) or, as an alternative thereto, the corresponding amide, i.e. niacinamide or nicotinamide (also known as vitamin PP) for the treatment of various forms of primary **headache**, such as classical migraine or migraine with an aura, common migraine or migraine without an aura, complicated migraine and cluster **headache** or histamine **headache**. The invention also concerns compositions for the treatment of primary **headaches** which are based on the two aforesaid active ingredients.

Excerpt(s): The present invention concerns the use of a vitamin combination for the treatment of primary **headaches**. More particularly, this invention relates to the use of a combination of two vitamin compounds, i.e. riboflavin (also known as vitamin B.sub.2) and nicotinic acid (also referred to as niacin) or, as an alternative thereto, the corresponding amide, i.e. niacinamide or nicotinamide (also known as vitamin PP) for the treatment of various forms of primary, headaches, among which common migraine, classical migraine or migraine with aura, duster headache and complicated migraine. Once having excluded that the symptoms are linked to a different basic disorder, then it is likely that the disorder is one of the possible arms of primary headaches, often referred to as a "migraine", which affect about 20-30% of the population (prevalently women). According to one of the current classifications, this may be of one of the following four forms: 1) classical migraine, i.e. with an aura; 2) common migraine, i.e. without an aura; complicated migraine; 4) cluster headache. Apart from the cluster headache, the aforesaid other forms of migraine generally consist of a pulsating periodic headache affecting one half of the cranium, and often associated with nausea and/or vomiting. The disorder generally starts in childhood, during adolescence and early adulthood and decreases in intensity and frequency over the years. In particular, a classical migraine starts with the so-called aura, consisting of protracted neurological symptoms for 30 minutes and includes photophobia, flashing scotoma (ie. bright flashing sensations before the eyes, with jagged edging similar to a wall), vertigo and tinnitus. With common migraines the headache arise with-out a prior aura, but often involves nausea or vomiting. Complicated migraines are instead characterised by headaches associated with particular neurological symptoms that may precede or accompany them. In particular, there may be paresthesia and hypoesthesia of the lips, face, hand and leg of al hemi-soma, sometimes associated with aphasic disorders, or one end of an arm or leg may become hyposthenic or plegic simulating an ictus. The sensitive disorders or feelings of weakness extend slowly from one side of the body to the other for a period a few minutes. Usually, after an attack, there in a complete return to normality, but there may also be permanent deficiencies among which hemianopsia, hemiplegia and hemianestesia. Cluster headache, also referred to as paroxysmal

nocturnal **headache**, hemicranial neuralgia, histamine **headache** and Horton's syndrome, is four times more common in men than in women, and is characterised by a constant unilateral orbital pain generally beginning two or three hours after sleep onset. The pain is intense and steady but not pulsating, and involves lachrymation, nasal congestion, rhinorrhea and then myosis, reddening and oadema of the cheek that lasts for about 30 an hour. This form of **headache** tends to occur cyclically during the right for several weeks or months (hence the name "cluster") and is then followed by a complete recovery for months or even years. Episodes of cluster **headache** of 2-3 week duration may arise several times in a lifetime.

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# • Use of BIBN4096 in combination with other antimigraine drugs for the treatment of migraine

Inventor(s): Doods, Henri; (Warthausen, DE), Eberlein, Wolfgang; (Biberach, DE), Rudolf, Klaus; (Warthausen, DE)

Correspondence: Boehringer Ingelheim Corporation; 900 Ridgebury Road; P. O. Box 368; Ridgefield; CT; 06877; US

Patent Application Number: 20030181462

Date filed: August 13, 2002

Abstract: A method of treatment or prevention of **headache**, migraine or cluster **headaches**, which method comprises co-administration of a therapeutically effective amount of the compound 1-[N.sup.2-[3,5-dibromo-N-[[4-(3,4-dihyd- ro-2(1H)-oxochinazolin-3-yl)-1-piperidinyl]-carbonyl]-D-tyrosyl]-L-lysyl]-- 4-(4-pyridinyl)-piperazine[BIBN4096BS] or a physiologically acceptable salt thereof and a therapeutically effective amount of a second active antimigraine drug, particularly sumatriptan, zolmitriptan or dihydroergotamin or a physiologically acceptable salt thereof, as well as to the corresponding pharmaceutical compositions and the preparation thereof.

Excerpt(s): Benefit of U.S. provisional application Ser. No. 60/315,321, filed Aug. 28, 2001 is hereby claimed. This is a continuation-in-part of Attorney Docket No. 1/1248 filed on Aug. 9, 2002. The invention relates to a method for the treatment or prevention of **headache**, migraine and cluster **headaches**, which comprises the co-administration of the agent BIBN4096BS and another antimigraine drug. Migraine is one of the most common neurological disorders, involving periodical attacks of **headache** and nausea as well as a plethora of other symptoms. Although considerable progress has been made, the pathophysiology of migraine is still not understood. However, several observations point to an involvement of Calcitonin Gene-Related Peptide (CGRP). Migraine **headache** involves the activation of the trigeminal system and dilatation of cranial vessels. CGRP is localized to neurons in the trigeminal ganglia and CGRP levels are increased during a migraine attack, presumably causing the vasodilation observed. Accordingly, it is conceivable that inhibition of CGRP-evoked dilatation of the cranial vessels may provide a novel treatment for migraine **headache**.

### • Vanilloid receptor ligands and their use in treatments

Inventor(s): Bo, Yunxin Y.; (Thousand Oaks, CA), Chakrabarti, Partha P.; (Simi Valley, CA), Chen, Ning; (Thousand Oaks, CA), Doherty, Elizabeth M.; (Newbury Park, CA), Fotsch, Christopher H.; (Thousand Oaks, CA), Han, Nianhe; (Thousand Oaks, CA), Kelly, Michael G.; (Thousand Oaks, CA), Liu, Qingyian; (Camarillo, CA), Norman, Mark Henry; (Thousand Oaks, CA), Ognyanov, Vassil I.; (Thousand Oaks, CA), Wang, Xianghong; (Moorpark, CA), Zhu, Jiawang; (Simi Valley, CA)

Correspondence: U.S Patent Operations/rvp; DEPT. 4300, M/s 27-4-a; Amgen INC.; One Amgen Center Drive; Thousand Oaks; CA; 91320-1799; US

Patent Application Number: 20030195201

Date filed: December 10, 2002

Abstract: Compounds having the general structure 1and compositions containing them, for the treatment of acute, inflammatory and neuropathic pain, dental pain, general **headache**, migraine, cluster **headache**, mixed-vascular and non-vascular syndromes, tension **headache**, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders.

Excerpt(s): This application claims the benefit of U.S. Provisional Application Nos. 60/339,161 filed Dec. 10, 2001, 60/344,737, filed Dec. 21, 2001, 60/383,331, filed May 22, 2002 and 60/402,422, filed Aug. 8, 2002, which are hereby incorporated by reference. The vanilloid receptor 1 (VR1) is the molecular target of capsaicin, the active ingredient in hot peppers. Julius et al. reported the molecular cloning of VR1 (Caterina et al., 1997). VR1 is a non-selective cation channel which is activated or sensitized by a series of different stimuli including capsaicin and resiniferatoxin (exogenous activators), heat & acid stimulation and products of lipid bilayer metabolism, anandamide (Premkumar et al., 2000, Szabo et al., 2000, Gauldie et al., 2001, Olah et al., 2001) and lipoxygenase metabolites (Hwang et al., 2000). VR1 is highly expressed in primary sensory neurons (Caterina et al., 1997) in rats, mice and humans (Onozawa et al., 2000, Mezey et al., 2000, Helliwell et al., 1998, Cortright et al., 2001). These sensory neurons innervate many visceral organs including the dermis, bones, bladder, gastrointestinal tract and lungs; VR1 is also expressed in other neuronal and non-neuronal tissues including but not limited to, CNS nuclei, kidney, stomach and T-cells (Nozawa et al., 2001, Yiangou et al., 2001, Birder et al., 2001). Presumably expression in these various cells and organs may contribute to their basic properties such as cellular signaling and cell division. Prior to the molecular cloning of VR1, experimentation with capsaicin indicated the presence of a capsaicin sensitive receptor, which could increase the activity of sensory neurons in humans, rats and mice (Holzer, 1991; Dray, 1992, Szallasi and Blumberg 1996, 1999). The results of acute activation by capsaicin in humans was pain at injection site and in other species increased behavioral sensitivity to sensory stimuli (Szallasi and Blumberg, 1999). Capsaicin application to the skin in humans causes a painful reaction characterized not only by the perception of heat and pain at the site of administration but also by a wider

area of hyperalgesia and allodynia, two characteristic symptoms of the human condition of neuropathic pain (Holzer, 1991). Taken together, it seems likely that increased activity of VR1 plays a significant role in the establishment and maintenance of pain conditions. Topical or intradermal injection of capsaicin has also been shown to produce localized vasodilation and edema production (Szallasi and Blumberg 1999, Singh et al., 2001). This evidence indicates that capsaicin through it's activation of VR1 can regulate afferent and efferent function of sensory nerves. Sensory nerve involvement in diseases could therefore be modified by molecules which effect the function of the vanilloid receptor to increase or decrease the activity of sensory nerves.

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

#### Zonisamide use in headache

Inventor(s): Jennings, Julianne E.; (San Diego, CA)

Correspondence: Howrey Simon Arnold & White, Llp; Box 34; 301 Ravenswood AVE.; Menlo Park; CA; 94025; US

Patent Application Number: 20030036556

Date filed: June 28, 2002

Abstract: The present invention is directed to a method of treating **headache**, including migraine. The method comprises administering to a subject a pharmaceutical composition comprising an effective amount of zonisamide. The methods of the present invention are useful in relieving **headache**. The compounds of the present method can also be used in conjunction with other therapeutic agents commonly used to treat **headache** thus enhancing the therapeutic effect of reducing **headache**.

Excerpt(s): The present invention relates to methods of treating **headache**, particularly migraine headache, with zonisamide (1,2-benzioxazole-3-metha- nesulfonamide). Migraine headache ("migraine") is a common disorder, believed to afflict 20 to 30 percent of the population, some transiently, some chronically. In migraine patients, throbbing head pain occurs at intervals. The pain often is associated with symptoms such as nausea, vomiting and impaired vision. The biochemical mechanisms underlying migraine are uncertain. The predominate belief expressed in the literature for many years has been that vasodilation of extracranial vessels causes migraine. Treatment efforts, therefore, were aimed at methods of causing vasoconstriction. More recently, evidence has shown that activation of prejunctional 5-HT.sub.1 heteroreceptors on primary afferent trigeminovascular fibers, by drugs such as ergot alkaloids and sumatriptan, alleviate migraine pain, suggesting a neuronal pathogenesis as opposed to a vascular one. Trigeminovascular fibers innervate meningeal blood vessels. The interaction of these compounds with the 5-HT1 receptor is very specific. These compounds do not interact with other 5-HT receptors, norepinephrine receptors, glutamate receptors or GABA (gamma-aminobutyric acid) receptors (Moskowitz, et. al., Annu. Rev. Med. 44:145-54 (1993)).

# **Keeping Current**

In order to stay informed about patents and patent applications dealing with headache, you can access the U.S. Patent Office archive via the Internet at the following Web address: **http://www.uspto.gov/patft/index.html**. You will see two broad options: (1) Issued Patent, and (2) Published Applications. To see a list of issued patents, perform the following steps: Under "Issued Patents," click "Quick Search." Then, type "headache" (or synonyms) into the "Term 1" box. After clicking on the search button, scroll down to see the various patents which have been granted to date on headache.

You can also use this procedure to view pending patent applications concerning headache. Simply go back to **http://www.uspto.gov/patft/index.html**. Select "Quick Search" under "Published Applications." Then proceed with the steps listed above.

# **CHAPTER 7. BOOKS ON HEADACHE**

# Overview

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

### • Orofacial Pain with a Neurological or Vascular Background

Source: in Scully, C. Handbook of Oral Disease: Diagnosis and Management. New York, NY: Thieme New York. 2001. p.39-52.

Contact: Available from Thieme New York. 333 Seventh Avenue, New York, NY 10001. (212) 760-0888, ext 110. PRICE: \$35.00 plus shipping and handling. ISBN: 1841840874.

Summary: Pain is the most common oral complaint. Usually it has a local cause, but neurological (nervous system), vascular (blood vessel), psychogenic (of psychological cause), and other causes should be excluded. This chapter on orofacial pain with a neurological or vascular background is from a handbook of oral disease that is intended to be used by all members of the dental team who need a ready office reference. The handbook covers the more common and important soft tissue orofacial disorders and gives clinically relevant aspects of the etiology, diagnosis, treatment, and prevention. This chapter covers causalgia (a persistent burning pain that follows surgery or trauma),
cranial arteritis (also called temporal arteritis or giant-cell arteritis); Frey's syndrome, a burning pain, usually in the temporal area in front of the ear, associated with flushing and sweating on eating; glossopharyngeal neuralgia; herpetic and postherpetic neuralgia, which is pain that persists after herpes zoster (shingles); migraine, a severe **headache** associated with nausea and sometimes photophobia (light sensitivity); migrainous neuralgia or cluster **headache**; referred pain; and trigeminal neuralgia. For each condition, the authors note etiology (cause), diagnosis, symptoms, epidemiology, risk factors, treatment, and prevention (where possible). Much of the information is provided in table format for ease of reference. Full color photographs illustrate some conditions. 4 figures. 2 tables. 25 references.

#### • Orofacial Pain: Guidelines for Assessment, Diagnosis, and Management

Source: Carol Stream, IL: Quintessence Publishing Company, Inc. 1996. 295 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: \$28.00 plus shipping and handling. ISBN: 0867153121.

Summary: This book discusses the assessment, diagnosis, and management of all pain conditions associated with the orofacial pain structures. Some areas, such as temporomandibular disorders (TMD), are presented in great detail and have been updated to integrate new scientific information. Other orofacial pain areas are presented in less detail to give the practitioner insight on their relationships in the assessment and diagnosis of orofacial pain. Ten chapters cover an introduction to orofacial pain, the assessment of orofacial pain disorders, a diagnostic classification of orofacial pain disorders, and the differential diagnosis and management considerations of vascular and nonvascular intracranial disorders; primary **headache**; neuralgias, nerve trunk pain, and deafferentation pain; intraoral pain disorders; temporomandibular disorders; associated structures that can produce orofacial pain; and mental disorders. The book concludes with an extensive glossary of terms and a subject index. (AA-M).

#### Diabetes Problem Solver

Source: Alexandria, VA: American Diabetes Association. 1999. 511 p.

Contact: Available from American Diabetes Association (ADA). Order Fulfillment Department, P.O. Box 930850, Atlanta, GA 31193-0850. (800) 232-6733. Fax (770) 442-9742. Website: www.diabetes.org. PRICE: \$19.95 for members; plus shipping and handling. ISBN: 1570400091.

Summary: This book is a reference guide that helps people who have diabetes identify and prevent the most common diabetes-related problems they encounter on a daily basis. The book is divided into two major sections. The first section consists of a series of flowcharts to help readers decide what they need to do about a particular condition or symptom. Flowcharts focus on arm and hand pain, back pain, blurry vision, chest pain, confusion, convulsions or seizures, difficulty breathing, dizziness, dry skin, eating disorders, emotional problems, emotional changes in women, feeling tired, fever, foot problems, **headache**, hyperglycemia, hypoglycemia, injection site problems, and intestinal problems. Other flowcharts deal with leg and foot pain, loss of consciousness, muscular weakness, nausea, numbness and tingling, pain or discomfort in women, palpitations, problems with the mouth, problems with blood glucose in women, sexual problems in men and women, skin discoloration, skin lesions, skin rashes and itchy skin, sleeping problems, stomach pain, sweating, swelling, thickening of the skin, urinary problems, vision problems, and vomiting. The second section provides more detailed information about many of the problems people who have diabetes face. Solutions are provided for monitoring and testing problems; hypoglycemia and hyperglycemia problems; insulin delivery and oral medication problems; circulation, neuropathy, kidney, vision, gastrointestinal, infection, foot, and skin problems; men's, women's, and children's problems; eating, exercise, and weight problems; lifestyle problems; coping problems; discrimination and insurance problems; and other medical problems. Each section provides the reader with information on the symptoms of the condition, who is at risk and what risk the particular condition poses for the reader, what the reader's immediate course of action should be, treatment in a medical setting, and how to prevent the condition from developing. The reader may use the book in two ways. If the reader knows he or she has a particular condition or wants more information, he or she can go straight to the second section and look up the condition. The reader may use the book as a guide to possible conditions that may be causing symptoms by referring to the flowcharts in the first section. The book also includes a glossary, resources, and an index. 6 figures. 5 tables.

# • Food Allergy Book: The Foods That Cause You Pain and Discomfort and How to Take Them Out of Your Diet

Source: St. Paul, MN: ACA Publications, Inc. 1995. 202 p.

Contact: Available from ACA Publications, Inc. 1690 University Avenue West, Suite 450, St. Paul, MN 55104. (800) 649-3523 or (612) 649-3523. Fax (612) 649-3509. PRICE: \$12.95. ISBN: 0963154478.

Summary: This book provides information about identifying and managing food allergies. The author describes the role that food allergy may play in migraine **headache**, sinus congestion and **headache**, stuffy nose, persistent cough, recurring sore throats, canker sores, wheezing, hives, eczema, persistent muscle and joint aching, recurring abdominal pain, diarrhea, tiredness, and irritability. The author reviews the hows and whys of food allergy and describes how certain commonly eaten foods can cause illness. Specific chapters discuss citrus, monosodium glutamate (MSG), low-calorie sweeteners, refined sugar, an adult and child allergy elimination diet, living with a restricted diet, reading food labels, shopping, meal planning and preparation, snack foods, and eating out in restaurants. A final chapter outlines a recommended diet for identifying and eliminating food allergy triggers. The book concludes with a bibliography and a subject index. 32 references.

#### • Understanding Impacted Wisdom Teeth

Source: Chicago, IL: Quintessence Publishing Co, Inc. 1998. 31 p.0.

Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: \$26.00 plus shipping and handling. ISBN: 08671532400.

Summary: This patient education booklet offers readers facts about wisdom teeth, how they develop, how they become impacted, and why they are often removed. Written in a question and answer format, the booklet covers why some people have impacted wisdom teeth and some do not, how to determine the best time to have wisdom teeth removed, and the consequences for older people who still have impacted wisdom teeth. The booklet also explores problems that may be encountered with impacted wisdom teeth, including gum infection, bone infection, infection that breaks through the bone into the cheek or neck, damage to other teeth, cysts, tooth or facial pain, earache or **headache**, and tooth movement. The descriptions are written in non technical language and each concept is illustrated with a full color anatomical drawing.

#### • Medical Problems in Dentistry. 4th ed

Source: Woburn, MA: Butterworth-Heinemann. 1998. 570 p.

Contact: Available from Butterworth-Heinemann. 225 Wildwood Avenue, Woburn, MA 01801-2041. (800) 366-2665 or (781) 904-2500. Fax (800) 446-6520 or (781) 933-6333. E-mail: orders@bhusa.com. Website: www.bh.com. PRICE: \$110.00. ISBN: 0723610568.

Summary: This text covers the general medical and surgical conditions relevant to the oral health care sciences. In providing a basis for the understanding of how these disorders influence oral health and oral health care, the text helps dental staff become aware of a variety of medical problems. Twenty-seven chapters cover medical history and assessment, perioperative care, cardiovascular disease, disorders of hemostasis, anemia, malignant disease, cytotoxic chemotherapy and radiotherapy, respiratory disorders, gastrointestinal disorders, liver disease, infections and infection control, skin diseases, genitourinary and renal disease, endocrine conditions, metabolic conditions and nutrition, musculoskeletal disorders, neurologic disorders, psychiatric disorders, headache and orofacial pain, immunodeficiencies, immunologically mediated disease, maxillofacial trauma and head injury, patients with disabilities, children and the elderly, chemical dependence, reactions to drugs and materials, drug interactions, emergencies, and socioeconomic, ethnic and geographic health issues. One appendix addresses miscellaneous uncommon or rare disorders of possible relevance to dentistry, not included elsewhere in the text. Each chapter includes references and a 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 "headache" at online booksellers' Web sites, you may discover <u>non-medical books</u> that use the generic term "headache" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "headache" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- "My Tummy Has a Headache": Helping Children Understand Illness by Desmond Spiers, Beverley Mathias (1993); ISBN: 0948664150; http://www.amazon.com/exec/obidos/ASIN/0948664150/icongroupinterna
- 311C90: Futher Advances in the Pathogenesis and Acute Treatment of Migraine: 7th International Headache Congress, Toronto, Canada, September 20, 1995 (Journal -European Neurology, Vol 36, Suppl 2) by J. G. Edmeads (Editor), M. D. Ferrari (Editor) (1996); ISBN: 3805563310; http://www.amazon.com/exec/obidos/ASIN/3805563310/icongroupinterna
- **50 Natural Ways to Cure a Headache** by Raje Airey (2002); ISBN: 0754809994; http://www.amazon.com/exec/obidos/ASIN/0754809994/icongroupinterna

- A Headache in the Pelvis: A New Understanding and Treatment for Prostatitis and Chronic Pelvic Pain Syndromes, Second Edition by David Wise, Rodney Anderson (2003); ISBN: 097277551X; http://www.amazon.com/exec/obidos/ASIN/097277551X/icongroupinterna
- A Pain Specialist's Approach to the Headache Patient by Seymour, M.D. Diamond, Prithvi P. Raj (Designer) (1993); ISBN: 0823639304; http://www.amazon.com/exec/obidos/ASIN/0823639304/icongroupinterna
- Advanced Therapy in Headache by Purdy, B C Decker (2004); ISBN: 1550092529; http://www.amazon.com/exec/obidos/ASIN/1550092529/icongroupinterna
- Aleutian Headache: Deadly World War II Battles on American Soil (Documentary) by Bert Webber (2003); ISBN: 0936738693; http://www.amazon.com/exec/obidos/ASIN/0936738693/icongroupinterna
- Alivio Rapido Del Dolor De Cabeza Sin Medicamentos/Quick Headache Relief Without Drugs by Howard Kurland (1981); ISBN: 8425310350; http://www.amazon.com/exec/obidos/ASIN/8425310350/icongroupinterna
- Alternative Medicine Definitive Guide to Headaches by Robert D. Milne, et al (1996); ISBN: 1887299033; http://www.amazon.com/exec/obidos/ASIN/1887299033/icongroupinterna
- An Atlas of Headache by Stephen D. Silberstein (Editor), et al; ISBN: 185070547X; http://www.amazon.com/exec/obidos/ASIN/185070547X/icongroupinterna
- Botulinum Toxin in Painful Diseases (Pain and Headache, 14) by W. H. Jost (Editor) (2003); ISBN: 3805575009; http://www.amazon.com/exec/obidos/ASIN/3805575009/icongroupinterna
- Breaking the Headache Cycle : A Proven Program for Treating and Preventing Recurring Headaches by Ian Livingstone (Author), Donna Novak (Author) (2004); ISBN: 0805072217;
  Isson (Author) (2004) (20050502015);
  Isson (Author) (2004) (2004);
  Isson (Author) (2004) (2004) (2004);
  Isson (Author) (2004) (2004) (2004);
  Isson (Author) (2004) (20

http://www.amazon.com/exec/obidos/ASIN/0805072217/icongroupinterna

- Business Doctor: How to Turn Your Headache Business into a Debt-Free Money Machine by Arnold S. Goldstein, Mark T. Lauer (Editor) (1994); ISBN: 188053925X; http://www.amazon.com/exec/obidos/ASIN/188053925X/icongroupinterna
- Childhood Headache by Ishaq Abu-Arafeh (Editor), Mac Keith Press (Editor) (2002); ISBN: 1898683263; http://www.amazon.com/exec/obidos/ASIN/1898683263/icongroupinterna
- Chronic Headache Vol. 1., Vol. 1 by Charles W. Theisler (1990); ISBN: 0683048821; http://www.amazon.com/exec/obidos/ASIN/0683048821/icongroupinterna
- Clinicians Guide to Headache by Isis Press, et al (2003); ISBN: 1901865894; http://www.amazon.com/exec/obidos/ASIN/1901865894/icongroupinterna
- Cluster Headache Syndrome in General Practice: Basic Concepts by Ottar Sjaastad (Editor), Giuseppe Nappi (Editor) (2000); ISBN: 1854632159; http://www.amazon.com/exec/obidos/ASIN/1854632159/icongroupinterna
- Cluster Headache: Mechanisms and Management by Lee Kudrow; ISBN: 0192611690; http://www.amazon.com/exec/obidos/ASIN/0192611690/icongroupinterna
- Cluster Headaches: Treatment and Relief for Cluster, Cluster Migraine, and Recurring Eyestab Pain by Michael E. Goldstein (1999); ISBN: 1881217183; http://www.amazon.com/exec/obidos/ASIN/1881217183/icongroupinterna

- Conquer Your Headaches: How to Get Rid of Your Headaches and on With Your Life by Robert G., Md. Ford, Kay T. Ford (Contributor) (1994); ISBN: 0963629255; http://www.amazon.com/exec/obidos/ASIN/0963629255/icongroupinterna
- Coping With Migraines and Other Headaches (Coping Library) by Andrea Votava (1997); ISBN: 0823925668; http://www.amazon.com/exec/obidos/ASIN/0823925668/icongroupinterna
- Coping With Your Headaches by Seymour Diamond (1988); ISBN: 0823610837; http://www.amazon.com/exec/obidos/ASIN/0823610837/icongroupinterna
- Critical Decisions in Headache Management by David W. Dodick, et al (2004); ISBN: 1550092448;
  - http://www.amazon.com/exec/obidos/ASIN/1550092448/icongroupinterna
- Daily Chronic Headache by Goadsby (2004); ISBN: 1550092650; http://www.amazon.com/exec/obidos/ASIN/1550092650/icongroupinterna
- Diagnosis and Management of Pain in Patients With Cancer (Pain and Headache, Vol 10) by Ronald Kanner (1988); ISBN: 3805546904; http://www.amazon.com/exec/obidos/ASIN/3805546904/icongroupinterna
- Dr. Ho's Hands-On Solutions to Neck, Shoulder, and Headache Problems by Michael, Dr. Ho (2003); ISBN: 1550225375; http://www.amazon.com/exec/obidos/ASIN/1550225375/icongroupinterna
- Drug Induced Headache (1988); ISBN: 3540187626; http://www.amazon.com/exec/obidos/ASIN/3540187626/icongroupinterna
- Drug Treatment of Migraine and Other Headaches by Hans Chr. Diener (Author) (2000); ISBN: 3805569718; http://www.amazon.com/exec/obidos/ASIN/3805569718/icongroupinterna
- Eighteen Natural Ways to Beat a Headache (1986); ISBN: 9990395942; http://www.amazon.com/exec/obidos/ASIN/9990395942/icongroupinterna
- Everything You Need to Know About Migraines and Other Headaches by Barbara Moe (2000); ISBN: 0823932915; http://www.amazon.com/exec/obidos/ASIN/0823932915/icongroupinterna
- Feverfew: Natural Headache Relief (Woodland Health Series) by Deanne Tenney (1998); ISBN: 1580540120; http://www.amazon.com/exec/obidos/ASIN/1580540120/icongroupinterna
- Free Yourself from Headaches by Jan Stromfield, Anita Weil (1995); ISBN: 0452262577; http://www.amazon.com/exec/obidos/ASIN/0452262577/icongroupinterna
- Free Yourself from Headaches: The Natural Drug-Free Program for Prevention and Relief by Anita Weil (Contributor), Jan, Dr. Stromfeld (1995); ISBN: 1883319315; http://www.amazon.com/exec/obidos/ASIN/1883319315/icongroupinterna
- Freedom from Headaches by J. Dr. Saper, et al (1986); ISBN: 0671254049; http://www.amazon.com/exec/obidos/ASIN/0671254049/icongroupinterna
- Handbook of Headache Disorders by Arthur H. Elkind (1994); ISBN: 0929240561; http://www.amazon.com/exec/obidos/ASIN/0929240561/icongroupinterna
- Handbook of Headache Management: A Practical Guide to Diagnosis & Treatment of Head, Neck & Facial Pain by Joel R. Saper (Editor), et al (1999); ISBN: 0781720486; http://www.amazon.com/exec/obidos/ASIN/0781720486/icongroupinterna

- **Headache** by Egiluis L. H. Spierings, Egilius L. H. Spierings (1998); ISBN: 0750671289; http://www.amazon.com/exec/obidos/ASIN/0750671289/icongroupinterna
- Headache (1968); ISBN: 3540162046; http://www.amazon.com/exec/obidos/ASIN/3540162046/icongroupinterna
- **Headache** by Neil H. Raskin; ISBN: 0721674674; http://www.amazon.com/exec/obidos/ASIN/0721674674/icongroupinterna
- Headache & Other Head Pain Ed.Dalessio 4/E by Harold G. Wolff, Donald J. Dalessio (Editor) (1993); ISBN: 0195026241; http://www.amazon.com/exec/obidos/ASIN/0195026241/icongroupinterna
- Headache (Clinical Medicine and the Nervous System) by Richard C. Peatfield (1968); ISBN: 0387162046; http://www.amazon.com/exec/obidos/ASIN/0387162046/icongroupinterna
- **Headache and Facial Pain** by Franco Mongini (1999); ISBN: 3131165413; http://www.amazon.com/exec/obidos/ASIN/3131165413/icongroupinterna
- Headache in Primary Care by Stephen D., Md. Silberstein (Editor), et al (1999); ISBN: 1901865665;

http://www.amazon.com/exec/obidos/ASIN/1901865665/icongroupinterna

- Headache Relief by Seymour, Md Diamond, et al (2000); ISBN: 1567313884; http://www.amazon.com/exec/obidos/ASIN/1567313884/icongroupinterna
- Headache Relief for Women by Fred Alan/Sheftell Rapoport (Author) (1996); ISBN: 0316733911; http://www.amazon.com/exec/obidos/ASIN/0316733911/icongroupinterna
- Headache Survival: The Holistic Medical Treatment Program for Migraine, Tension, and Cluster Headaches by Robert S. Ivker, et al (2002); ISBN: 1585421413; http://www.amazon.com/exec/obidos/ASIN/1585421413/icongroupinterna
- Headache: Health & Medical Subject Subject Analysis With Reference Bibliography by Paula Nesta Aggerholm (1986); ISBN: 0881644846; http://www.amazon.com/exec/obidos/ASIN/0881644846/icongroupinterna
- Headache: Hope Through Research by National Institute Of Neurological Disor (1996); ISBN: 0160488567; http://www.amazon.com/exec/obidos/ASIN/0160488567/icongroupinterna
- Headache: Problems in Diagnosis & Management by Anthony Hopkins (1997); ISBN: 0039190161;

http://www.amazon.com/exec/obidos/ASIN/0039190161/icongroupinterna

- Headache: Problems in Diagnosis and Management (Major Problems in Neurology, Vol 15) by Anthony Hopkins (Editor) (1988); ISBN: 003910916X; http://www.amazon.com/exec/obidos/ASIN/003910916X/icongroupinterna
- Headaches (My Health) by Alvin Silverstein, et al (2001); ISBN: 053111872X; http://www.amazon.com/exec/obidos/ASIN/053111872X/icongroupinterna
- Headaches (Sound Techniques for Healing) by Robert Friedman, Kelly Howell (1993); ISBN: 1881451186; http://www.amazon.com/exec/obidos/ASIN/1881451186/icongroupinterna
- Homeopathy for Headaches: Ursula Stone by Ursula Stone (1999); ISBN: 1575664178; http://www.amazon.com/exec/obidos/ASIN/1575664178/icongroupinterna

- Hope for Your Headache Problem: More Than Two Aspirin by Seymour Diamond, Amy D. Vye (1988); ISBN: 0823623505; http://www.amazon.com/exec/obidos/ASIN/0823623505/icongroupinterna
- How Does Aspirin Find a Headache? by David Feldman (Author) (1994); ISBN: 0060925582;

http://www.amazon.com/exec/obidos/ASIN/0060925582/icongroupinterna

- I Think, Therefore I Have a Headache: A Laugh-Out-Loud Look at Life by Martha Bolton (2003); ISBN: 0764226258; http://www.amazon.com/exec/obidos/ASIN/0764226258/icongroupinterna
- Management of Chronic Headaches: A Psychological Approach (Psychology Practitioner Guidebooks) by Edward B. Blanchard, F. Andraisk (1992); ISBN: 0205142850;

http://www.amazon.com/exec/obidos/ASIN/0205142850/icongroupinterna

• Management of Headache and Headache Medications by Lawrence D. Robbins (2000); ISBN: 0387989447;

http://www.amazon.com/exec/obidos/ASIN/0387989447/icongroupinterna

- Manual Therapy for Chronic Headache by Joy Edeling (1988); ISBN: 0407005609; http://www.amazon.com/exec/obidos/ASIN/0407005609/icongroupinterna
- Me + Math = Headache (Pullet Book from Red Hen Press) by Lee, Wardlaw, et al (1986); ISBN: 0931093074; http://www.amazon.com/exec/obidos/ASIN/0931093074/icongroupinterna
- Mechanism and Management of Headache by James W. Lance, Peter J. Goadsby; ISBN: 0750637285; http://www.amazon.com/exec/obidos/ASIN/0750637285/icongroupinterna
- Mechanisms and Management of Headache by James W. Lance (1982); ISBN: 0407264582;

http://www.amazon.com/exec/obidos/ASIN/0407264582/icongroupinterna

- Migraine and Headache in Children by Vincenzo Guidetti, George Russell; ISBN: 1853178101; http://www.amazon.com/exec/obidos/ASIN/1853178101/icongroupinterna
- Migraine and Other Headaches: A Practical Guide to Understanding, Preventing and Treating Headaches by James W. Lance (1998); ISBN: 0731807405; http://www.amazon.com/exec/obidos/ASIN/0731807405/icongroupinterna
- Migraine and Other Headaches: Your Questions Answered by Andrew J. Dowson (2003); ISBN: 0443073392; http://www.amazon.com/exec/obidos/ASIN/0443073392/icongroupinterna
- Mommy, My Head Hurts: A Doctor's Guide to Your Child's Headache by Sarah Cheyette (2002); ISBN: 1557045356; http://www.amazon.com/exec/obidos/ASIN/1557045356/icongroupinterna
- **My Favorite Headache** by Geddy Lee, Ben Mink (2001); ISBN: 075790758X; http://www.amazon.com/exec/obidos/ASIN/075790758X/icongroupinterna
- Natural & Herbal Remedies for Headaches (Storey Country Wisdom Bulletin, A-265) by Elizabeth Wotton (2001); ISBN: 1580173497; http://www.amazon.com/exec/obidos/ASIN/1580173497/icongroupinterna

- Neurosurgical Treatment of Persistent Pain: Physiological and Pathological Mechanisms of Human Pain (Pain and Headache, Vol 11) by Jan M. Gybels, William H. Sweet (1989); ISBN: 3805548850; http://www.amazon.com/exec/obidos/ASIN/3805548850/icongroupinterna
- Neurotransmitters and Pain Control (Pain and Headache, Vol 9) by H. Akil, J.W. Lewis (Editor) (1987); ISBN: 3805545797; http://www.amazon.com/exec/obidos/ASIN/3805545797/icongroupinterna
- New Advances in Headache Research by F. Clifford Rose (Editor) (1994); ISBN: 1854630946; http://www.amazon.com/exec/obidos/ASIN/1854630946/icongroupinterna
- No Headache Guide to Home Repair Series by Douglas Emley (1995); ISBN: 1884348068; http://www.amazon.com/exec/obidos/ASIN/1884348068/icongroupinterna
- Okay, So I Don't Have a Headache by Cristina Ferrare (2000); ISBN: 031226366X; http://www.amazon.com/exec/obidos/ASIN/031226366X/icongroupinterna
- Pain and Profits: The History of the Headache and Its Remedies in America by Janice Rae McTavish (2004); ISBN: 0813534402; http://www.amazon.com/exec/obidos/ASIN/0813534402/icongroupinterna
- Pain in Peripheral Nerve Diseases (Pain and Headache, Vol 13) by C. Sommer (Editor) (2001); ISBN: 3805572689; http://www.amazon.com/exec/obidos/ASIN/3805572689/icongroupinterna
- Pain System (Pain and Headache, Vol 8) by William D. Willis (1985); ISBN: 3805539304; http://www.amazon.com/exec/obidos/ASIN/3805539304/icongroupinterna
- Pathophysiologic, Diagnostic & Therapeutic Aspects of Headache by Mary E. Granger (Editor) (1976); ISBN: 3805522827; http://www.amazon.com/exec/obidos/ASIN/3805522827/icongroupinterna
- Pediatric and Young Adult Headache Management by Winner (2004); ISBN: 1550092960; http://www.amazon.com/exec/obidos/ASIN/1550092960/icongroupinterna
- Pointers to the Common Remedies: Vertigo, Headache, Apoplexy, Sleeplessness, Collapse, Sunstroke by M.L. Tyler (1981); ISBN: 0946717516; http://www.amazon.com/exec/obidos/ASIN/0946717516/icongroupinterna
- Reducing the Burden of Headache by J. Olesen (Editor), et al (2003); ISBN: 0198515898; http://www.amazon.com/exec/obidos/ASIN/0198515898/icongroupinterna
- Self-Massage for Your Headache (Chinese Health Library Series) by Simon Wang (1998); ISBN: 0964160587; http://www.amazon.com/exec/obidos/ASIN/0964160587/icongroupinterna
- Stop Headaches Now: Headaches Can Be Stopped Without Drugs and Without Surgery by Jerry Simin, Jerry M. Simon (2001); ISBN: 1587410796; http://www.amazon.com/exec/obidos/ASIN/1587410796/icongroupinterna
- Take the Bite Out of Headache Pain: Accurate Diagnosis & Proper Treatment of Temporomandibular Joint (Tmj) Dysfunction Is the Natural Solution to Many Pain & Dental Symptoms [UNABRIDGED] by Jerry Simon (2001); ISBN: 0966619501; http://www.amazon.com/exec/obidos/ASIN/0966619501/icongroupinterna

- The Child With Headache: Diagnosis & Treatment (Progress in Pain Research and Management, V. 19) by Patricia A. McGrath (Editor), Loretta M. Hillier (Editor) (2001); ISBN: 0931092302; http://www.amazon.com/exec/obidos/ASIN/0931092302/icongroupinterna
- The Chronic Pain Patient: Evaluation and Management (Pain and Headache, Vol 7) by Philip L. Gildenberg, R. A. Devaul (Editor) (1984); ISBN: 3805539118; http://www.amazon.com/exec/obidos/ASIN/3805539118/icongroupinterna
- The Headache & Neck Pain Workbook: An Integrated Mind and Body Program by Douglas E. Degood, et al (1997); ISBN: 1572240865; http://www.amazon.com/exec/obidos/ASIN/1572240865/icongroupinterna
- The Headache Book (1994); ISBN: 0840782564; http://www.amazon.com/exec/obidos/ASIN/0840782564/icongroupinterna
- The Headache Ort Stage 2 6-Pack by Hunt (1985); ISBN: 0198491891; http://www.amazon.com/exec/obidos/ASIN/0198491891/icongroupinterna
- The Ice-Cream Headache & Other Stories by James Jones, Kaylie Jones (Preface) (2002); ISBN: 1888451351; http://www.amazon.com/exec/obidos/ASIN/1888451351/icongroupinterna
- The Initial Processing of Pain and Its Descending Control: Spinal and Trigeminal Systems (Pain and Headache, Vol 12) by Alan R. Light (1992); ISBN: 3805555695; http://www.amazon.com/exec/obidos/ASIN/3805555695/icongroupinterna
- The Practicing Physician's Approach to Headache (1992); ISBN: 0683025058; http://www.amazon.com/exec/obidos/ASIN/0683025058/icongroupinterna
- The Sexual Aspects of Headaches by Seymour Diamond (Editor), Michael Maliszewski (Editor) (1992); ISBN: 0823660710; http://www.amazon.com/exec/obidos/ASIN/0823660710/icongroupinterna
- The Triptans: Novel Drugs for Migraine (Frontiers in Headache Research Series, 10) by Patrick Humphrey (Editor), et al (2002); ISBN: 0192632140; http://www.amazon.com/exec/obidos/ASIN/0192632140/icongroupinterna
- The Zero-G Headache (Astrokids, No 2) by Robert Elmer (2000); ISBN: 0764223577; http://www.amazon.com/exec/obidos/ASIN/0764223577/icongroupinterna
- Treating Sinus, Migraine, and Cluster Headaches, My Way : An allergist's approach to headache treatment by William E. Walsh MD (1993); ISBN: 0963154451; http://www.amazon.com/exec/obidos/ASIN/0963154451/icongroupinterna
- Understanding Headaches and Migraines by Mark Forshaw (Author) (2004); ISBN: 0470847603;

http://www.amazon.com/exec/obidos/ASIN/0470847603/icongroupinterna

- Understanding Migraine and Other Headaches (Understanding Health and Sickness Series) by Stewart J., M.D. Tepper (2004); ISBN: 1578065917; http://www.amazon.com/exec/obidos/ASIN/1578065917/icongroupinterna
- Updating in Headache (Proceedings of 1st International Headache Congress, Munich) by V. Pfaffenrath, et al (1985); ISBN: 0387153187; http://www.amazon.com/exec/obidos/ASIN/0387153187/icongroupinterna
- Who Needs Headaches by Cass Dr Igram, et al (1991); ISBN: 0911119329; http://www.amazon.com/exec/obidos/ASIN/0911119329/icongroupinterna

• Wolff's Headache and Other Head Pain by Harold G. Wolff (Editor), et al; ISBN: 0195135180; http://www.amazon.com/avac/abidac/ASIN/0195135180/icongroupinterna

http://www.amazon.com/exec/obidos/ASIN/0195135180/icongroupinterna

# The National Library of Medicine Book Index

The National Library of Medicine at the National Institutes of Health has a massive database of books published on healthcare and biomedicine. Go to the following Internet site, **http://locatorplus.gov/**, and then select "Search LOCATORplus." Once you are in the search area, simply type "headache" (or synonyms) into the search box, and select "books only." From there, results can be sorted by publication date, author, or relevance. The following was recently catalogued by the National Library of Medicine:<sup>11</sup>

- Drug trials for headache; principles and methods. Prepared for National Institute of Neurological Diseases and Blindness, by the Ad Hoc Committee on Headache, Arnold P. Friedman, chairman. Author: Ad Hoc Committee on Headache.; Year: 1954; [Bethesda, Md.] National Institute of Neurological Diseases and Blindness, 1968
- Headache and other head pain. Author: Wolff, Harold G. (Harold George),; Year: 1967; New York, Oxford Univ. Press, 1972
- Headache. Author: National Institute of Neurological Diseases and Stroke.; Year: 1966; Bethesda, Md., For sale by the Supt. of Docs., U. S. Govt. Print. Off., Washington, 1969]
- Headaches and cranial neuralgias. Edited by P. J. Vinken and G. W. Bruyn. Author: Vinken, P. J.; Year: 1957; Amsterdam, North-Holland Pub. Co.; New York, Wiley Interscience Division [1968]
- Headaches in children; comp. and ed. by Arnold P. Friedman and Ernest Harms, with contributions by Abby Adams [et al.]. Author: Friedman, Arnold P. (Arnold Phinehas),; Year: 1968; Springifeld, Ill., Thomas [c1967]
- Headaches; the kinds and the cures. Author: Freese, Arthur S.,; Year: 1966; Garden City, N. Y., Doubleday, 1973; ISBN: 0385039662 http://www.amazon.com/exec/obidos/ASIN/0385039662/icongroupinterna
- **Post-lumbar puncture headaches, by Wallace W. Tourtellotte [et al.].** Author: Tourtellotte, Wallace W.; Year: 1967; Springfield, Ill., Thomas [c1964]
- The mechanism and management of headache. Author: Lance, James W. (James Waldo); Year: 1964; London, Butterworth [c1969]; ISBN: 407264558
- Treatment of headache; guest editor: Arnold P. Friedman. Treatment of acid peptic disease; guest editor: Howard M. Spiro. Author: Friedman, Arnold P. (Arnold Phinehas),; Year: 1966; [New York] Harper; Row, 1964

<sup>&</sup>lt;sup>11</sup> In addition to LOCATORPlus, in collaboration with authors and publishers, the National Center for Biotechnology Information (NCBI) is currently adapting biomedical books for the Web. The books may be accessed in two ways: (1) by searching directly using any search term or phrase (in the same way as the bibliographic database PubMed), or (2) by following the links to PubMed abstracts. Each PubMed abstract has a "Books" button that displays a facsimile of the abstract in which some phrases are hypertext links. These phrases are also found in the books available at NCBI. Click on hyperlinked results in the list of books in which the phrase is found. Currently, the majority of the links are between the books and PubMed. In the future, more links will be created between the books and other types of information, such as gene and protein sequences and macromolecular structures. See http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books.

# Chapters on Headache

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

#### • Cervical Synovial Joints as Sources of Post-Traumatic Headache

Source: in Allen, M.E., Ed. Musculoskeletal Pain Emanating From the Head and Neck: Current Concepts in Diagnosis, Management and Cost Containment. Binghamton, NY: The Haworth Medical Press. 1996. p. 81-94.

Contact: Haworth Document Delivery Service, Haworth Press, Inc., 10 Alice Street, Binghamton, NY 13904-1580. (800) 342-9678. (800) 895-0582 (fax).

Summary: This chapter for health professionals reviews research which elucidates the role of the cervical synovial joints as sources of pain in patients with posttraumatic headache. Recent research has demonstrated that the cervical synovial joints are innervated and that they can be potent sources of neck pain and headache if stimulated in normal subjects or if injured in patients. Postmortem studies of injured joints have revealed chondral and subchondral fractures, bruising or damage of the intra-articular inclusions, hemarthroses, and capsular tears or avulsions. These acute lesions constitute the substrate for the development of posttraumatic arthritis and, consequently, chronic posttraumatic headache. Such lesions evade detection by conventional diagnostic techniques. However, the advent of innovative diagnostic approaches, including manipulative assessment, biomechanical analysis, and controlled diagnostic injection techniques, has allowed the identification of painful cervical synovial joints in vivo. Using these diagnostic techniques, epidemiological studies have shown that the cervical zygapophysial joints are common sources of posttraumatic headache. Findings support the hypothesis that cervical synovial joint pain is a real and common clinical entity. Controlled diagnostic blocks are the only reliable means whereby this condition can be identified. They provide a criterion standard against which other diagnostic techniques could be calibrated in the future. 56 references and 5 figures. (AA-M).

# **CHAPTER 8. MULTIMEDIA ON HEADACHE**

#### Overview

In this chapter, we show you how to keep current on multimedia sources of information on headache. 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.

#### **Audio Recordings**

The Combined Health Information Database contains abstracts on audio productions. To search CHID, go directly to the following hyperlink: http://chid.nih.gov/detail/detail.html. To find audio 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 "Sound Recordings." Type "headache" (or synonyms) into the "For these words:" box. The following is a typical result when searching for sound recordings on headache:

#### • AIDS Update: ED Management, Part II

Contact: California Medical Association, Audio Digest Foundation, 1577 E Chevy Chase Dr, Glendale, CA, 91206, (213) 245-8505.

Summary: This sound recording, along with accompanying pre-test and post-test questions, comprises part of an ongoing series of educational activities. The first speaker, George F. Risi Jr., Assistant Professor of Medicine at Louisiana State University School of Medicine in New Orleans, looks at the evolution of the Acquired immunodeficiency syndrome (AIDS) epidemic between 1981 and 1986. He discusses the test for Human immunodeficiency virus (HIV) antibodies, HIV transmission, early theories about the origin of the illness, and the Centers for Disease Control and Prevention (CDC) classification system for AIDS patients. David F. Dreis, of the Section of Chest and Infectious Diseases at Virginia Mason Medical Center in Seattle, looks at symptoms and opportunistic infections associated with AIDS in the second presentation. He examines Pneumocystis carinii pneumonia (PCP), Candida Albicans, Kaposi's sarcoma, decreased vision, **headache**, unexplained fever, leukoplakia, pulmonary diseases, cryptosporidium, toxoplasmosis, and tuberculosis (TB). Asymptomatic carriers are discussed.

# **Bibliography: Multimedia on Headache**

The National Library of Medicine is a rich source of information on healthcare-related multimedia productions including slides, computer software, and databases. To access the multimedia database, go to the following Web site: **http://locatorplus.gov/**. Select "Search LOCATORplus." Once in the search area, simply type in headache (or synonyms). Then, in the option box provided below the search box, select "Audiovisuals and Computer Files." From there, you can choose to sort results by publication date, author, or relevance. The following multimedia has been indexed on headache:

- Acute idiopathic headache [videorecording]: Rx for success Source: CME-TV; produced in cooperation with University of Arizona Health Sciences Center; Year: 1991; Format: Videorecording; Hagerman, Idaho: CME-TV, c1991
- Advanced therapy of headache Source: Alan M. Rapoport, Fred D. Sheftell, R. Allan Purdy; Year: 1999; Format: Edited by; Hamilton [Ont.]; Saint Louis: Decker, c1999
- **Cephalalgia: an international journal of headache.** Year: 9999; Oslo: Universitetsforlaget
- Critical decisions in headache management Source: Rose Giammarco, John Edmeads, David Dodick; Year: 1998; Hamilton: B.C. Decker; Malden, MA, USA: Sales and distribution, US, Blackwell Science, 1998
- Diagnosis & management of headache [videorecording] Source: a Hahnemann Medical College & Hospital and World Video Corp. production; Year: 1981; Format: Videorecording; [S.l.]: Analgesic CME Group, c1981
- **Diagnostic approach to headaches [sound recording]** Source: Dept. of Continuing Medical Education, School of Medicine, State University of New York at Buffalo, in cooperation with the Lakes Area Regional Medical Program; Year: 1974; Format: Sound recording; [Buffalo]: Communications in Learning, 1974
- Headache & facial pain [sound recording]: diagnostic measures & surgical treatment modalities Source: American College of Surgeons; Year: 1980; Format: Sound recording; [Chicago]: The College, [1980]
- **Headache [videorecording]** Source: Council on Continuing Physician Education; Year: 1979; Format: Videorecording; Chicago: AMA, c1979
- **Headache** [videorecording] Source: Martin A. Samuels; Year: 1996; Format: Videorecording; Los Angeles, CA: Mayer Media, 1996
- Headaches [electronic resource]: a diagnostic and management challenge Source: by Harvey J. Featherstone; Year: 1985; Format: Electronic resource; [Seattle, Wash.]: CME, c1985
- Headaches [videorecording] Source: Emory University School of Medicine; Year: 1977; Format: Videorecording; Atlanta: Georgia Regional Medical Television Network: [for loan or sale by A. W. Calhoun Medical Library, 1977]
- **Headaches [videorecording]** Source: a joint production of. Audio Visual Center and Staff Education; Year: 1993; Format: Videorecording; [Oakland, Calif.]: Kaiser Foundation Health Plan, c1993
- **Headaches [videorecording]** Source: Time Life Medical; produced in association with Sonalysts Studios; Year: 1996; Format: Videorecording; New York, NY: Patient Education Media, c1996

- Headaches [videorecording] Source: co-production of Multimedia Communications and Physician Education and Development; Year: 1999; Format: Videorecording; Oakland, CA: Kaiser Foundation Health Plan, c1999
- Headaches in adults and children [videorecording] Source: CME Conference Video, Inc.; sponsored by the Cleveland Clinic Foundation; Year: 1994; Format: Videorecording; Mt. Laurel, NJ: CME Conference Video, 1994
- Management of headaches [videorecording] Source: [presented by] the Medical University of South Carolina, College of Medicine and the Health Communications Network; produced by the Health Communications Network, Division of Television Services, Medical Univers; Year: 1992; Format: Videorecording; Charleston, S.C.: The University, c1992
- Management of organic headache [videorecording] Source: Washington Alaska Regional Medical Program; produced by Information & Education Resource Support Unit, University of Washington School of Medicine; Year: 1970; Format: Videorecording; [Washington, D.C.: National Audiovisual Center, 1970?]
- Mechanisms of tension type headache, myofascial pain, migraine [videorecording]; Is there such a thing as TMJ headache Source: Nineteenth Annual Scientific Meeting on Orofacial Pain and Temporomandibular Disorders; produced on location by Teach'em; Year: 1994; Format: Videorecording; [Chicago, IL: Teach'em, 1994]
- Medical treatment of headache [videorecording] Source: a production of the Office of Health Extension, Public Service and Research for the University of Alabama School of Medicine, Department of Neurology; Year: 1981; Format: Videorecording; Carrboro, NC: Health Sciences Consortium, c1981
- No more headaches [videorecording] Source: developed in cooperation with the National Headache Foundation and Carnrick Laboratories, Inc; Year: 1992; Format: Videorecording; Andover, MA: Xenejenex Productions, c1992
- **Pitfalls and pointers in the management of chronic headaches [videorecording]** Source: with Larry S. Eisner; Year: 1985; Format: Videorecording; Secaucus, N.J.: Network for Continuing Medical Education, 1985
- **Recurrent headache [videorecording]** Source: [presented by] Marshfield Clinic, Saint Joseph's Hospital [and] Marshfield Medical Research Foundation; Year: 1990; Format: Videorecording; Marshfield, WI: Marshfield Video Network, [1990]
- Treating headaches with homeopathic medicines [sound recording] Source: Nat'l Center for Homeopathy, Los Angeles 1990; Year: 1990; Format: Sound recording; Berkeley, CA: Conference Recording Service, [1990]

# **CHAPTER 9. PERIODICALS AND NEWS ON HEADACHE**

#### Overview

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

#### **News Services and Press Releases**

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

- Harry Potter causing Hogwarts headaches? Source: Reuters Health eLine Date: October 30, 2003
- Treatment available for "orgasmic headaches" Source: Reuters Health eLine Date: October 01, 2003

- Other benign headache types linked to headache associated with sexual activity Source: Reuters Medical News Date: September 30, 2003
- Next-generation mobile signals shown to cause nausea, headache Source: Reuters Medical News Date: September 30, 2003
- **3G mobile signals cause nausea, headache survey** Source: Reuters Health eLine Date: September 30, 2003
- Too much soda may cause caffeine headaches in kids Source: Reuters Health eLine Date: June 24, 2003
- Chronic headaches may predict men's stroke risk Source: Reuters Health eLine Date: May 29, 2003
- Trigeminal nerve sectioning may be a valid option for chronic cluster headache Source: Reuters Medical News Date: May 09, 2003
- Parenteral indomethacin does not prevent cluster headache Source: Reuters Industry Breifing Date: May 02, 2003
- Snoring may be risk factor for chronic daily headache Source: Reuters Medical News Date: April 21, 2003
- Snoring linked to chronic daily headache: study Source: Reuters Health eLine Date: April 21, 2003
- Nonheadache premonitory symptoms predict migraine onset Source: Reuters Medical News Date: April 18, 2003

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

#### • Headaches!

Source: Lupus News. 16(4):1,4-6.

Contact: Lupus Foundation of America, Inc. Western Pennsylvania Chapter, 1323 Forbes Ave. Suite 200, Pittsburgh, PA 15219. (412)261-5886. Fax 412-261-5365. 1 (800)-800-5776.

Summary: This newsletter article for individuals with systemic lupus erythematosus (SLE) explains when and how headache may reflect underlying lupus activity. Types of headaches are identified, including muscle contraction headache, common and classic migraine, cluster headache, and other. Their presumed causes include sustained muscle contractions around the face and head, inflammation of the lining of the sinuses of the

nose and head, eye strain, pain from the temporal mandibular joint, and major changes in the brain. The role that psychological factors have in the manifestation of headaches and pain in general is examined. Symptoms that may represent a manifestation of SLE are identified. Suggested treatments for headaches are offered.

#### • Headaches in Ehlers-Danlos Syndrome

Source: Loose Connections. XV(3): 1,4-8. September-October 2000.

Contact: Available from Ehlers-Danlos National Foundation. 6399 Wilshire Blvd., Suite 510, Los Angeles, CA 90048. (323) 651-3038.

Summary: This newsletter article provides health professionals and people who have Ehlers-Danlos syndrome (EDS) with information on a study that investigated the occurrence of chronic headaches in this complex hereditary connective tissue disorder. Data were obtained from 18 patients with EDS and chronic headaches. All of the patients were seen in a rural practice setting and were followed for a minimum of 2 years. Procedures included clinical history taking, neurologic examination, computerized tomography of the head, magnetic resonance imaging of the brain, and electroencephalogram (EEG). Headaches were classified according to the International Headache Society. The study found that four patients had migraine with aura, four had migraine without aura, four had tension headaches, four had a combination of migraine and tension headaches, and two had posttraumatic headaches. Nine patients exhibited blepharoclonus, but none had a history of seizures and their EEGs were normal, ruling out eye closure epilepsy. Although one patient had a small right frontal angioma, a second had Arnold Chiari malformation type I, and a third had an old stroke, headaches did not clinically correlate with their central nervous system (CNS) lesions. The article concludes that chronic recurrent headaches may constitute the neurologic presentation of EDS in the absence of structural, congenital, or acquired CNS lesions that correlate with their symptoms. People who have EDS may be prone to migraine due to an inherent disorder of cerebrovascular reactivity or cortical excitability. Additional studies are needed to elucidate the pathogenesis of headaches in EDS. 1 table and 5 references. (AA-M).

#### • Understanding Headaches

Source: Fibromyalgia Frontiers. 7(5): 5-7. September-October 1999.

Contact: Available from National Fibromyalgia Partnership. 140 Zinn Way, Linden, VA 22642-5609. Toll-free phone (866) 725-4404. Fax (540) 622-2998. E-mail: mail@fmpartnership.org. Website: www.fmpartnership.org.

Summary: This newsletter article provides people who have fibromyalgia (FM) with information on the treatment of primary headache disorders. These uncomfortable disorders are usually benign. Although each headache syndrome has its own distinctive pain patterns, vascular headaches and tension headaches have overlaps in treatment. The mainstays of preventive medication in the treatment of vascular headaches and tension headaches are the tricyclics and beta blockers. Selective serotonin uptake inhibitors, which are sometimes helpful in FM, probably help tension headaches more than vascular headaches. The physical approach to the management of vascular headaches is also helpful in treating the patient with FM. Although tension like headaches are believed to be caused by muscle contraction, in patients with FM they may also be related to neurally mediated hypotension. Temporomandibular joint dysfunction (TMD) is very common in these patients, and treatment is similar to that given to others who have TMD. Atypical facial pain syndromes may be more common

in patients with FM than in the general population. Other head pain syndromes such as cluster headache and trigeminal neuralgia are no more common in patients with FM than in the general population, so treatments are specific to the particular disorder. People who experience headaches, particularly those who have FM, need to avoid narcotics and other drugs that can cause rebound headaches.

#### Headaches After Acoustic Neuroma Surgery

Source: ANA Notes. Number 75: 1, 8-10. March 2001.

Contact: Available from Acoustic Neuroma Association (ANA). 600 Peachtree Parkway, Suite 108, Cumming, GA 30041-8211. (770) 205-8211. Fax (770 www.ANAUSA.org.

Summary: This newsletter article reports on the incidence of headaches after acoustic neuroma surgery. The author notes that although headaches as a symptom prior to treatment are relatively uncommon for vestibular schwannoma, they occur with surprising frequency after treatment and can have a profound impact upon quality of life in acoustic neuroma patients. The pain often persists for prolonged periods of time and does not always respond well to a number of medical and surgical treatments directed at the headache. The author discusses the frequency of headache following neuroma surgery, the nature of the headache, their causes, and current therapies. Causes of the headaches can include the surgical approach (craniectomy versus craniotomy), aspetic meningitis, muscle pain, nerve entrapment, and low cerebrospinal fluid pressure. The best treatment is prevention, since these headaches have proven to be difficult to treat once they occur. The author also discusses the use of cranioplasty, medication, local therapy to neck muscles, nerve block or section, stress reduction and antidepressants, and care from a multidisciplinary pain center. The author notes that most surgeons are aware of the need to prevent these headaches and take measures to minimize muscle incisions, to replace skull bone whenever possible, and to limit the distribution of bone dust within the operative field.

#### Academic Periodicals covering Headache

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to headache. In addition to these sources, you can search for articles covering headache that have been published by any of the periodicals listed in previous chapters. To find the latest studies published, go to **http://www.ncbi.nlm.nih.gov/pubmed**, type the name of the periodical into the search box, and click "Go."

If you want complete details about the historical contents of a journal, you can also visit the following Web site: http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi. Here, type in the name of the journal or its abbreviation, and you will receive an index of published articles. At http://locatorplus.gov/, you can retrieve more indexing information on medical periodicals (e.g. the name of the publisher). Select the button "Search LOCATORplus." Then type in the name of the journal and select the advanced search option "Journal Title Search."

# **CHAPTER 10. RESEARCHING MEDICATIONS**

#### Overview

While a number of hard copy or CD-ROM resources are available for researching medications, a more flexible method is to use Internet-based databases. Broadly speaking, there are two sources of information on approved medications: public sources and private sources. We will emphasize free-to-use public sources.

#### U.S. Pharmacopeia

Because of historical investments by various organizations and the emergence of the Internet, it has become rather simple to learn about the medications recommended for headache. One such source is the United States Pharmacopeia. In 1820, eleven physicians met in Washington, D.C. to establish the first compendium of standard drugs for the United States. They called this compendium the U.S. Pharmacopeia (USP). Today, the USP is a non-profit organization consisting of 800 volunteer scientists, eleven elected officials, and 400 representatives of state associations and colleges of medicine and pharmacy. The USP is located in Rockville, Maryland, and its home page is located at http://www.usp.org/. The USP currently provides standards for over 3,700 medications. The resulting USP DI® Advice for the Patient<sup>®</sup> can be accessed through the National Library of Medicine of the National Institutes of Health. The database is partially derived from lists of federally approved medications in the Food and Drug Administration's (FDA) Drug Approvals database, located at http://www.fda.gov/cder/da/da.htm.

While the FDA database is rather large and difficult to navigate, the Phamacopeia is both user-friendly and free to use. It covers more than 9,000 prescription and over-the-counter medications. To access this database, simply type the following hyperlink into your Web browser: http://www.nlm.nih.gov/medlineplus/druginformation.html. To view examples of a given medication (brand names, category, description, preparation, proper use, precautions, side effects, etc.), simply follow the hyperlinks indicated within the United States Pharmacopeia (USP).

Below, we have compiled a list of medications associated with headache. If you would like more information on a particular medication, the provided hyperlinks will direct you to ample documentation (e.g. typical dosage, side effects, drug-interaction risks, etc.). The following drugs have been mentioned in the Pharmacopeia and other sources as being potentially applicable to headache:

#### Acetaminophen and Salicylates

• Systemic - U.S. Brands: Note: http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203003.html

#### Antidepressants, Monoamine Oxidase (Mao) Inhibitor

• Systemic - U.S. Brands: Marplan; Nardil; Parnate http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202054.html

#### Antidepressants, Tricyclic

• **Systemic - U.S. Brands:** Anafranil; Asendin; Aventyl; Elavil; Endep; Norfranil; Norpramin; Pamelor; Sinequan; Surmontil; Tipramine; Tofranil; Tofranil-PM; Vivactil

http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202055.html

#### Antihistamines

• Systemic - U.S. Brands: Aller-Chlor; AllerMax Caplets; Aller-med; Atarax; Banophen; Banophen Caplets; Benadryl; Benadryl Allergy; Bromphen; Calm X; Chlo-Amine; Chlorate; Chlor-Trimeton; Chlor-Trimeton Allergy; Chlor-Trimeton Repetabs; Claritin; Claritin Reditabs; Compoz; Conta http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202060.html

#### Antihistamines, Decongestants, and Analgesics

• Systemic - U.S. Brands: Aclophen; Actifed Cold & Sinus; Actifed Cold & Sinus Caplets; Actifed Sinus Nighttime; Actifed Sinus Nighttime Caplets; Alka-Seltzer Plus Allergy Medicine Liqui-Gels; Alka-Seltzer Plus Cold Medicine; Alka-Seltzer Plus Cold Medicine Liqui-Gels; Allerest http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202062.html

#### Anti-Inflammatory Drugs, Nonsteroidal

• Systemic - U.S. Brands: Actron; Advil; Advil Caplets; Advil, Children's; Aleve; Anaprox; Anaprox DS; Ansaid; Bayer Select Ibuprofen Pain Relief Formula Caplets; Cataflam; Clinoril; Cotylbutazone; Cramp End; Daypro; Dolgesic; Dolobid; EC-Naprosyn; Excedrin IB; Excedrin IB Caple http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202743.html

#### Barbiturates, Aspirin, and Codeine

• Systemic - U.S. Brands: Ascomp with Codeine No.3; Butalbital Compound with Codeine; Butinal with Codeine No.3; Fiorinal with Codeine No.3; Idenal with Codeine; Isollyl with Codeine http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202104.html

#### Benzodiazepines

• Systemic - U.S. Brands: Alprazolam Intensol; Ativan; Dalmane; Diastat; Diazepam Intensol; Dizac; Doral; Halcion; Klonopin; Librium; Lorazepam Intensol; Paxipam; ProSom; Restoril; Serax; Tranxene T-Tab; Tranxene-SD; Tranxene-SD Half Strength; Valium; Xanax http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202084.html

#### **Beta-Adrenergic Blocking Agents**

• Systemic - U.S. Brands: Betapace; Blocadren; Cartrol; Corgard; Inderal; Inderal LA; Kerlone; Levatol; Lopressor; Normodyne; Sectral; Tenormin; Toprol-XL; Trandate; Visken; Zebeta http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202087.html

#### **Butalbital and Acetaminophen**

• Systemic - U.S. Brands: Note: http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202102.html

#### **Butalbital and Aspirin**

• **Systemic - U.S. Brands:** Axotal; Butalgen; Fiorgen; Fiorinal; Fiormor; Fortabs; Isobutal; Isobutyl; Isolin; Isollyl; Laniroif; Lanorinal; Marnal; Vibutal http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202103.html

#### Caffeine

• Systemic - U.S. Brands: Cafcit; Caffedrine Caplets; Dexitac Stay Alert Stimulant; Enerjets; Keep Alert; Maximum Strength SnapBack Stimulant Powders; NoDoz Maximum Strength Caplets; Pep-Back; Quick Pep; Ultra Pep-Back; Vivarin http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202105.html

#### **Calcium Channel Blocking Agents**

 Systemic - U.S. Brands: Adalat; Adalat CC; Calan; Calan SR; Cardene; Cardizem; Cardizem CD; Cardizem SR; Dilacor-XR; DynaCirc; Isoptin; Isoptin SR; Nimotop; Plendil; Procardia; Procardia XL; Vascor; Verelan http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202107.html

#### Clomiphene

• Systemic - U.S. Brands: Clomid; Milophene; Serophene http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202151.html

#### Clonidine

• Systemic - U.S. Brands: Catapres; Catapres-TTS http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202152.html

#### Cromolyn

• Oral - U.S. Brands: Gastrocrom http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202169.html

#### **Decongestants and Analgesics**

• Systemic - U.S. Brands: Actifed Sinus Daytime; Actifed Sinus Daytime Caplets; Advil Cold and Sinus; Advil Cold and Sinus Caplets; Alka-Seltzer Plus Sinus Medicine; Allerest No-Drowsiness Caplets; Aspirin-Free Bayer Select Sinus Pain Relief Caplets; BC Cold Powder Non-Drowsy Fo http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202184.html

#### Dihydroergotamine

• Nasal-Systemic - U.S. Brands: Migranal http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203569.html

#### **Ergoloid Mesylates**

• Systemic - U.S. Brands: Gerimal; Hydergine http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202215.html

#### Ergotamine, Belladonna Alkaloids, and Phenobarbital

• Systemic - U.S. Brands: Bellergal-S http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202217.html

#### **Estrogens and Progestins Oral Contraceptives**

• Systemic - U.S. Brands: Alesse; Brevicon; Demulen 1/35; Demulen 1/50; Desogen; Estrostep; Estrostep Fe; Genora 0.5/35; Genora 1/35; Genora 1/50; Intercon 0.5/35; Intercon 1/35; Intercon 1/50; Jenest; Levlen; Levlite; Levora 0.15/30; Lo/Ovral; Loestrin 1.5/30; Loestrin 1/20; Lo http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202228.html

#### Gemcitabine

• Systemic - U.S. Brands: Gemzar http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203038.html

#### Headache Medicines, Ergot Derivative-Containing

• **Systemic - U.S. Brands:** Cafergot; Cafertine; Cafetrate; D.H.E. 45; Ercaf; Ergo-Caff; Ergomar; Ergostat; Gotamine; Migergot; Wigraine http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202216.html

#### Influenza Virus Vaccine

• Systemic - U.S. Brands: FluShield; Fluvirin; Fluzone http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202297.html

#### Isometheptene, Dichloralphenazone, and Acetaminophen

 Systemic - U.S. Brands: Amidrine; Duradrin; I.D.A; Iso-Acetazone; Isocom; Midchlor; Midrin; Migquin; Migrapap; Migratine; Migrazone; Migrend; Migrex; Mitride

http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202306.html

#### Lithium

• Systemic - U.S. Brands: Cibalith-S; Eskalith; Lithane; Lithobid; Lithonate; Lithotabs

http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202330.html

#### Methysergide

• Systemic - U.S. Brands: Sansert http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202363.html

#### Metoclopramide

• Systemic - U.S. Brands: Octamide; Reglan http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202364.html

#### Midodrine

• Systemic - U.S. Brands: ProAmatine http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203640.html

#### Naratriptan

• Systemic - U.S. Brands: Amerge http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203513.html

#### Oseltamivir

• Systemic - U.S. Brands: Tamiflu http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500062.html

#### Pyridoxine (Vitamin B 6)

• Systemic - U.S. Brands: Beesix; Doxine; Nestrex; Pyri; Rodex http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202493.html

#### Ribavirin

• Systemic - U.S. Brands: Virazole http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202509.html

#### Rizatriptan

• **Systemic - U.S. Brands:** Maxalt; Maxalt-MLT http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203620.html

#### Salicylates

• Systemic - U.S. Brands: Acuprin 81; Amigesic; Anacin Caplets; Anacin Maximum Strength; Anacin Tablets; Anaflex 750; Arthritis Pain Ascriptin; Arthritis Pain Formula; Arthritis Strength Bufferin; Arthropan; Aspergum; Aspirin Regimen Bayer Adult Low Dose; Aspirin Regimen Bayer R http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202515.html

#### Sumatriptan

• Systemic - U.S. Brands: Imitrex http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202665.html

#### Valproic Acid

• Systemic - U.S. Brands: Depacon; Depakene; Depakote; Depakote Sprinkle http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202588.html

#### Zanamivir

• Inhalation--Systemic - U.S. Brands: Relenza http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500004.html

#### Zolmitriptan

• Systemic - U.S. Brands: Zomig http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203426.html

# **Commercial Databases**

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. Or, you may be able to access these sources from your local medical library.

#### Mosby's Drug Consult<sup>TM</sup>

Mosby's Drug Consult<sup>™</sup> database (also available on CD-ROM and book format) covers 45,000 drug products including generics and international brands. It provides prescribing information, drug interactions, and patient information. Subscription information is available at the following hyperlink: http://www.mosbysdrugconsult.com/.

#### PDRhealth

The PDR*health* database is a free-to-use, drug information search engine that has been written for the public in layman's terms. It contains FDA-approved drug information adapted from the Physicians' Desk Reference (PDR) database. PDR*health* can be searched by brand name, generic name, or indication. It features multiple drug interactions reports. Search PDR*health* at http://www.pdrhealth.com/drug\_info/index.html.

#### Other Web Sites

Drugs.com (**www.drugs.com**) reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. (**http://www.medletter.com/**) which allows users to download articles on various drugs and therapeutics for a nominal fee.

If you have any questions about a medical treatment, the FDA may have an office near you. Look for their number in the blue pages of the phone book. You can also contact the FDA through its toll-free number, 1-888-INFO-FDA (1-888-463-6332), or on the World Wide Web at **www.fda.gov**.

# APPENDICES

# **APPENDIX A. PHYSICIAN RESOURCES**

## Overview

In this chapter, we focus on databases and Internet-based guidelines and information resources created or written for a professional audience.

## **NIH Guidelines**

Commonly referred to as "clinical" or "professional" guidelines, the National Institutes of Health publish physician guidelines for the most common diseases. Publications are available at the following by relevant Institute<sup>12</sup>:

- 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/

<sup>&</sup>lt;sup>12</sup> 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.<sup>13</sup> 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:<sup>14</sup>

- **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

<sup>&</sup>lt;sup>13</sup> 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).

<sup>&</sup>lt;sup>14</sup> 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 Combined Health Information Database

A comprehensive source of information on clinical guidelines written for professionals is the Combined Health Information Database. You will need to limit your search to one of the following: Brochure/Pamphlet, Fact Sheet, or Information Package, and "headache" using Search" directly "Detailed option. the Go to the following hyperlink: 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 the publication date, select "All Years." Select your preferred language and the format option "Fact Sheet." Type "headache" (or synonyms) into the "For these words:" box. The following is a sample result:

# • Clinical Management of the HIV - Infected Adult: A Manual for Mid - Level Clinicians

Contact: University of Illinois at Chicago, Midwest AIDS Education and Training Center, 808 S Wood St M/C 779, Chicago, IL, 60612-7303, (312) 996-1373.

Summary: This manual contains the protocol for the management of the HIV-infected patient. It begins with health maintenance protocols, which allow the clinician to provide a standardized database for the assessment and treatment of HIV-related problems, including acute intervention and ongoing supportive care. The HIV-specific laboratory protocols provide a guideline for monitoring patients with HIV infection which identifies other co-infections and assists in tracking disease progression. The HIV-specific assessment tool is used to help clinicians and caretakers measure the patient's ability to carry out activities of daily living. Complaint-specific protocols cover the ears, nose and sinuses, mouth and throat, fever, **headache**, shortness of breath, and seizures. The disease-specific protocols include cervical disease, histoplasmosis, HIV-related cardiomyopathy, oral candidiasis, kaposi's sarcoma, and many other specific diseases. Neuropsychiatric protocols offer guidelines for the treatment of major depression, generalized anxiety disorders, panic disorder, suicide, and AIDS dementia complex. The manual concludes with a comprehensive drug protocol--this includes antiretroviral therapy and common HIV medications.

#### • AIDS - Related Cryptococcal Meningitis

Contact: US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Allergy and Infectious Diseases, 31 Center Dr MSC 2520, Bethesda, MD, 20892-2520, (301) 496-5717, http://www.niaid.nih.gov.

Summary: This report describes cryptococcal meningitis that is related to Acquired immunodeficiency syndrome (AIDS). It says that cryptococcal disease accounts for 5-8 percent of all opportunistic infections, and that it is caused by cryptococcus neoformans, a yeastlike fungus found in soil contaminated with bird excrement. Exposure is quite common, but it only manifests as a disease in those individuals with compromised immune systems. The fungus may infect numerous organs, particularly the skin, lungs, and meninges. As meningitis, it has the following symptoms: Fever, **headache**, fatigue,

nausea, and vomiting. It may also cause changes in behavior or personality, memory loss or confusion, and difficulty with coordination. Unless maintenance therapy continues, the relapse rate after initial treatment is 50-90 percent. Standard treatment consists of Amphotericin B intravenously for 10 weeks, possibly combined with oral flucytosine. Side effects may include kidney damage, high fever, severe chills, low blood pressure, a decrease in potassium levels, and depressed levels of red and white blood cells, and platelets. Another drug called fluconazole was recently approved for oral or intravenous use, and one called SCH 39304 is under study. At present, the National Institute of Allergy and Infectious Diseases (NIAID) has four meningitis clinical trials underway.

#### • Toxoplasmic Encephalitis

Contact: US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Allergy and Infectious Diseases, 31 Center Dr MSC 2520, Bethesda, MD, 20892-2520, (301) 496-5717, http://www.niaid.nih.gov.

Summary: This report discusses toxoplasmosis, specifically toxoplasmic encephalitis, found in persons with Human immunodeficiency virus (HIV) infection or Acquired immunodeficiency syndrome (AIDS). It says that 20 to 30 percent of adults in the U.S. become infected with Toxoplasma gondii at some point, but unless their immune systems become damaged, they manifest no symptoms. The parasite can be passed to humans by contact with the excrement of infected cats, or transmitted in undercooked meat from other infected animals. The infection can result in encephalitis, a lifethreatening disease, or it may cause inflammation of parts of the eye. Symptoms of encephalitis include mild headache, fever, and nervous system impairment, including neurologic problems, seizures, diminished alertness, and even coma. The standard therapy consists of pyrimethamine and sulfadiazine, but the side effects are so severe in 40 percent of patients that the treatment must be discontinued. The treatment suppresses blood-forming cells, and also may result in blood in the urine, fever, severe rashes, abdominal discomfort, headaches, and abnormalities in the liver. Preliminary studies are being done on a combination of clindamycin and pyrimethamine. The National Institute of Allergy and Infectious Diseases (NIAID) presently has seven clinical trials ongoing on treatment of toxoplasmosis.

#### • AIDS - Related Cryptosporidiosis

Contact: US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Allergy and Infectious Diseases, 31 Center Dr MSC 2520, Bethesda, MD, 20892-2520, (301) 496-5717, http://www.niaid.nih.gov.

Summary: This report examines the most devastating gastrointestinal infection associated with Acquired immunodeficiency syndrome (AIDS), the diarrhea caused by the protozoan Cryptosporidian. The parasite lives in cattle and other domestic animals and is excreted; infection occurs by coming into contact with the animal or the excrement. In a person with a normal immune system, this causes acute diarrhea with flulike intestinal symptoms that vanish in about a week without treatment. But for Persons with AIDS (PWA's), the infection can be quite serious. Along with chronic diarrhea, symptoms may include abdominal cramps, nausea, vomiting, fever, and **headache.** Weakness and weight loss may also occur. It may last weeks or months so that the fluid loss becomes life-threatening and spread to other digestive organs, such as the gallbladder. A variety of treatments have been tried, but none have been effective. Fluid and nutrients are usually given orally or intravenously to compensate for the fluid lost. Presently, several drugs are being tested, including spiramycin, diclazuril,

hyperimmune bovine colostrum, and a synthetic form of the hormone somatostatin. The National Institute of Allergy and Infectious Diseases (NIAID) is presently conducting one clinical trial on cryptosporidiosis.

#### • AIDS - Related Disseminated Histoplasmosis

Contact: US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Allergy and Infectious Diseases, 31 Center Dr MSC 2520, Bethesda, MD, 20892-2520, (301) 496-5717, http://www.niaid.nih.gov.

Summary: This report studies histoplasmosis in patients with Human immunodeficiency virus (HIV) infection or Acquired immunodeficiency syndrome (AIDS). A fungal disease which may disseminate to many organs, histoplasmosis may be present in the body for a long time. The infection is common in certain regions, such as the Midwest and the Caribbean, where residents inhale or ingest spores of the fungus Historians Capsulate. The disease begins as an acute illness akin to pneumonia or influenza, and may spread to the meninges, heart, and adrenal glands. Persons with AIDS (PWA's) usually respond to the standard treatment with intravenous amphotericin B, but in 80-90 percent of patients, it recurs within a year without maintenance therapy. However, side effects may include high fever, shaking chills, **headache**, nausea, loss of appetite, muscle and joint pain, suppression of blood-forming cells, depletion of potassium, and abnormal kidney function. Ketoconzale and Itraconazole are being considered as possible alternative drugs. The National Institute of Allergy and Infectious Diseases (NIAID) is presently conducting three clinical trials of these drugs.

# • Changing Issues in the Management of HIV Infection: Chronic Therapy of Early HIV Infection

Contact: World Health Communications Incorporated, 41 Madison Ave 40th Fl, New York, NY, 10010, (212) 679-6200, http://www.whci.com. British Overseas Development Administration, 94 Victoria St, London.

Summary: This report summarizes the discussion of a panel of physicians, nurses, and healthcare professionals involved in clinical studies of azidothymidine (AZT), also known as retrovir. The report opens with a section looking at the effectiveness of therapy with AZT. Side effects, including anemia, myopathy, lymphoma, **headache**, nausea, and fatigue are studied in the second section. The final two sections look at maintaining patients on continued therapy and tracking clinical and other information during therapy.

#### The NLM Gateway<sup>15</sup>

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.<sup>16</sup> To use the NLM Gateway, simply go to the search site at http://gateway.nlm.nih.gov/gw/Cmd.

<sup>&</sup>lt;sup>15</sup> Adapted from NLM: http://gateway.nlm.nih.gov/gw/Cmd?Overview.x.

<sup>&</sup>lt;sup>16</sup> 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).

Type "headache" (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.

Category	<b>Items Found</b>
Journal Articles	31649
Books / Periodicals / Audio Visual	821
Consumer Health	1032
Meeting Abstracts	421
Other Collections	8
Total	33931

#### **Results Summary**

#### HSTAT<sup>17</sup>

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.<sup>18</sup> 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.<sup>19</sup> Simply search by "headache" (or synonyms) at the following Web site: http://text.nlm.nih.gov.

#### Coffee Break: Tutorials for Biologists<sup>20</sup>

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.<sup>21</sup> 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.<sup>22</sup> 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/.

<sup>&</sup>lt;sup>17</sup> Adapted from HSTAT: http://www.nlm.nih.gov/pubs/factsheets/hstat.html.

<sup>&</sup>lt;sup>18</sup> The HSTAT URL is **http://hstat.nlm.nih.gov/**.

<sup>&</sup>lt;sup>19</sup> 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.

<sup>&</sup>lt;sup>20</sup> Adapted from http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html.

<sup>&</sup>lt;sup>21</sup> 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.

<sup>&</sup>lt;sup>22</sup> 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.
## **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/.

## The Genome Project and Headache

In the following section, we will discuss databases and references which relate to the Genome Project and headache.

#### **Online Mendelian Inheritance in Man (OMIM)**

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).<sup>23</sup> The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

To search the database, go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html**. Type "headache" (or synonyms) into the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. In particular, the option "Database Links" will search across technical databases that offer an abundance of information. The following is an example of the results you can obtain from the OMIM for headache:

- Benign Sexual Headache Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607504
- Cluster Headache, Familial Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?119915
- Hyperthermia, Cutaneous, with Headaches and Nausea Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?145590

<sup>&</sup>lt;sup>23</sup> Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

#### Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web categorizes each disorder by system site of the body. Go to http://www.ncbi.nlm.nih.gov/disease/, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to revisit it from time to time. The following systems and associated disorders are addressed:

- Cancer: Uncontrolled cell division.
  Examples: Breast and ovarian cancer, Burkitt lymphoma, chronic myeloid leukemia, colon cancer, lung cancer, malignant melanoma, multiple endocrine neoplasia, neurofibromatosis, p53 tumor suppressor, pancreatic cancer, prostate cancer, Ras oncogene, RB: retinoblastoma, von Hippel-Lindau syndrome.
  Web site: http://www.ncbi.nlm.nih.gov/disease/Cancer.html
- Immune System: Fights invaders. Examples: Asthma, autoimmune polyglandular syndrome, Crohn's disease, DiGeorge syndrome, familial Mediterranean fever, immunodeficiency with Hyper-IgM, severe combined immunodeficiency. Web site: http://www.ncbi.nlm.nih.gov/disease/Immune.html

Metabolism: Food and energy. Examples: Adreno-leukodystrophy, atherosclerosis, Best disease, Gaucher disease, glucose galactose malabsorption, gyrate atrophy, juvenile-onset diabetes, obesity, paroxysmal nocturnal hemoglobinuria, phenylketonuria, Refsum disease, Tangier disease, Tay-Sachs disease. Web site: http://www.ncbi.nlm.nih.gov/disease/Metabolism.html

- **Muscle and Bone:** Movement and growth. Examples: Duchenne muscular dystrophy, Ellis-van Creveld syndrome, Marfan syndrome, myotonic dystrophy, spinal muscular atrophy. Web site: http://www.ncbi.nlm.nih.gov/disease/Muscle.html
- Nervous System: Mind and body. Examples: Alzheimer disease, amyotrophic lateral sclerosis, Angelman syndrome, Charcot-Marie-Tooth disease, epilepsy, essential tremor, fragile X syndrome, Friedreich's ataxia, Huntington disease, Niemann-Pick disease, Parkinson disease, Prader-Willi syndrome, Rett syndrome, spinocerebellar atrophy, Williams syndrome. Web site: http://www.ncbi.nlm.nih.gov/disease/Brain.html
- Signals: Cellular messages. Examples: Ataxia telangiectasia, Cockayne syndrome, glaucoma, male-patterned baldness, SRY: sex determination, tuberous sclerosis, Waardenburg syndrome, Werner syndrome.

Web site: http://www.ncbi.nlm.nih.gov/disease/Signals.html

 Transporters: Pumps and channels. Examples: Cystic fibrosis, deafness, diastrophic dysplasia, Hemophilia A, long-QT syndrome, Menkes syndrome, Pendred syndrome, polycystic kidney disease, sickle cell anemia, Wilson's disease, Zellweger syndrome. Web site: http://www.ncbi.nlm.nih.gov/disease/Transporters.html

#### Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **3D Domains:** Domains from Entrez Structure, Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo
- Books: Online books, Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books
- Genome: Complete genome assemblies, Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome
- NCBI's Protein Sequence Information Survey Results: Web site: http://www.ncbi.nlm.nih.gov/About/proteinsurvey/
- Nucleotide Sequence Database (Genbank): Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide
- **OMIM:** Online Mendelian Inheritance in Man, Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM
- **PopSet:** Population study data sets, Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset
- **ProbeSet:** Gene Expression Omnibus (GEO), Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo
- Protein Sequence Database: Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein
- **PubMed:** Biomedical literature (PubMed), Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed
- Structure: Three-dimensional macromolecular structures, Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure
- **Taxonomy:** Organisms in GenBank, Web site: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=genome**, and then select the database that you would like to search. The databases available are listed in the drop box next to "Search." Enter "headache" (or synonyms) into the search box and click "Go."

#### Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database<sup>24</sup>

This online resource has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually

<sup>&</sup>lt;sup>24</sup> Adapted from the National Library of Medicine:

http://www.nlm.nih.gov/mesh/jablonski/about\_syndrome.html.

limited or completely omitted in existing reference sources due to space limitations of the printed form.

At http://www.nlm.nih.gov/mesh/jablonski/syndrome\_toc/toc\_a.html, you can search across syndromes using an alphabetical index. Search by keywords at http://www.nlm.nih.gov/mesh/jablonski/syndrome\_db.html.

#### The Genome Database<sup>25</sup>

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type "headache" (or synonyms) into the search box, and review the results. If more than one word is used in the search box, then separate each one with the word "and" or "or" (using "or" might be useful when using synonyms).

<sup>&</sup>lt;sup>25</sup> Adapted from the Genome Database: http://gdbwww.gdb.org/gdb/aboutGDB.html - mission.

## **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 headache 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 headache. 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 headache. 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 "headache":

• Other guides

#### Botox

http://www.nlm.nih.gov/medlineplus/botox.html

Chiropractic

http://www.nlm.nih.gov/medlineplus/chiropractic.html

#### Head and Brain Injuries

http://www.nlm.nih.gov/medlineplus/headandbraininjuries.html

#### Heat Illness

http://www.nlm.nih.gov/medlineplus/heatillness.html

Migraine http://www.nlm.nih.gov/medlineplus/migraine.html

Neck Disorders and Injuries http://www.nlm.nih.gov/medlineplus/neckdisordersandinjuries.html

**Refractive Errors** http://www.nlm.nih.gov/medlineplus/refractiveerrors.html

Sinusitis http://www.nlm.nih.gov/medlineplus/sinusitis.html

Within the health topic page dedicated to headache, the following was listed:

• General/Overviews

What You Should Know about Headache Source: American Council for Headache Education http://www.achenet.org/understanding

Diagnosis/Symptoms

#### Headaches: Self-Care Flowcharts Source: American Academy of Family Physicians http://familydoctor.org/flowcharts/502.html

Treatment

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) Source: Mayo Foundation for Medical Education and Research http://www.mayoclinic.com/invoke.cfm?id=PN00038

• Alternative Therapy

Have a Splitting Headache? Chiropractic Care Can Help Source: American Chiropractic Association http://www.acatoday.com/media/tips/headache.shtml • Nutrition

#### **Diet and Headache**

Source: National Headache Foundation http://www.headaches.org/consumer/topicsheets/diet\_headache.html

Specific Conditions/Aspects

#### **Cluster Headache**

Source: Mayo Foundation for Medical Education and Research http://www.mayoclinic.com/invoke.cfm?id=DS00487

#### Early Morning Awakening Headaches

Source: National Headache Foundation http://www.headaches.org/consumer/topicsheets/earlymorning.html

#### Headache and Sinus Disease

Source: American Rhinologic Society http://american-rhinologic.org/cgibin/menu.cgi?m=main.menu&state=1001125555100000001000000&citem=7&f=patie ntinfo.headache.phtml

#### Headaches and Allergies

Source: American College of Allergy, Asthma & Immunology http://www.medem.com/MedLB/article\_detaillb.cfm?article\_ID=ZZZ4H568I6C& sub\_cat=129

#### Headaches Caused by Viral Infections

Source: National Headache Foundation http://www.headaches.org/consumer/topicsheets/viralinfections.html

#### Hemicrania Continua

Source: National Institute of Neurological Disorders and Stroke http://www.ninds.nih.gov/health\_and\_medical/disorders/hemicrania\_continua.h tm

#### Paroxysmal Hemicrania

Source: National Institute of Neurological Disorders and Stroke http://www.ninds.nih.gov/health\_and\_medical/disorders/paroxysmal\_hemicrani a.htm

#### **Rebound Headache**

Source: Beth Israel Medical Center, Dept. of Pain Medicine and Palliative Care http://stoppain.org/pain\_medicine/rebound.html

#### Sexual Benign Headaches

Source: National Headache Foundation http://www.headaches.org/consumer/topicsheets/sexual.html

# SUNCT Headache (Short-Lasting, Unilateral, Neuralgiform with Conjunctival Injection and Tearing)

Source: National Institute of Neurological Disorders and Stroke http://www.ninds.nih.gov/health\_and\_medical/disorders/sunct.htm

#### **Tension-Type Headache**

Source: Mayo Foundation for Medical Education and Research http://www.mayoclinic.com/invoke.cfm?id=DS00304

#### **Unusual Headaches**

Source: Mayo Foundation for Medical Education and Research http://www.mayoclinic.com/invoke.cfm?id=HQ01574

#### **Vision Problems Causing Headaches?**

Source: Mayo Foundation for Medical Education and Research http://www.mayoclinic.com/invoke.cfm?id=BN00009

#### Children

Chronic Headaches in Kids: Medication and Behavior Modifications May Help Source: Mayo Foundation for Medical Education and Research http://www.mayoclinic.com/invoke.cfm?id=HQ00428

#### **Headache Triggers**

Source: American Council for Headache Education http://www.achenet.org/kids/triggers.php

#### Headaches in Children

Source: American Council for Headache Education http://www.achenet.org/kids/children.php

#### Kids and Headache: Treatment

Source: American Council for Headache Education http://www.achenet.org/kids/treatment.php

**Oooh, Your Aching Head!** Source: Nemours Foundation http://kidshealth.org/kid/ill\_injure/sick/headache.html

Why Does Eating Ice Cream Give Me a Headache? Source: Nemours Foundation http://kidshealth.org/kid/talk/qa/ice\_cream\_headache.html

• From the National Institutes of Health

#### Headache

Source: National Institute of Neurological Disorders and Stroke http://www.ninds.nih.gov/health\_and\_medical/disorders/headache.htm

#### Headache: Hope through Research

Source: National Institute of Neurological Disorders and Stroke http://www.ninds.nih.gov/health\_and\_medical/pubs/headache\_htr.htm

Latest News

## Migraine? Take 'Triptan' Sooner Rather Than Later

Source: 11/07/2003, Reuters Health http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory\_14566 .html

• Men

#### Headache, Stress and "Moods"

Source: American Council for Headache Education http://www.achenet.org/women/stress/

#### Taking Control of Headache

Source: American Council for Headache Education http://www.achenet.org/women/control.php

Will Using Oral Contraceptives Make My Headaches Worse? Source: American Council for Headache Education http://www.achenet.org/women/oral/worse.php

Organizations

American Council for Headache Education http://www.achenet.org/

National Institute of Neurological Disorders and Stroke http://www.ninds.nih.gov/

Women

Headache, Stress and "Moods" Source: American Council for Headache Education http://www.achenet.org/women/stress/

Taking Control of Headache Source: American Council for Headache Education http://www.achenet.org/women/control.php

Will Using Oral Contraceptives Make My Headaches Worse? Source: American Council for Headache Education http://www.achenet.org/women/oral/worse.php

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 headache. 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:

#### • Headaches and Biofeedback

Source: Dallas, TX: MyoData-TMJ and Stress Center. 1990. 30 p.

Contact: Available from MyoData-TMJ and Stress Center. P.O. Box 803394, Dallas, TX 75380. (800) 533-5121 or (214) 416-7676. PRICE: \$6.95 plus shipping and handling; bulk orders available. Item Number B103.

Summary: This booklet provides a guide to headaches and how they can be helped with biofeedback. Topics covered include common types of headaches and how they occur, including tension headaches, migraines, cluster headaches, headache of cervical (neck) origin, headaches of dental origin, and other headache types; the role of emotional anxiety and stress in muscle tension; evaluating the cause of headaches, including the interview, the use of a headache diary, physical examination, and the use of biofeedback for diagnosis; treatment strategies, including relaxation training, postural training, stretching, the generalization technique; what patients can do, including nutrition and exercise; and non-biofeedback approaches to headache treatment, including physical therapy, dental treatment, and psychology. The brochure begins with a pre-test and concludes with a brief reading list. 6 references.

#### • Headache: Following Acoustic Neuroma Surgery Can Be a Real Pain in the Neck

Source: Atlanta, GA: Acoustic Neuroma Association (ANA). February 1996. 20 p.

Contact: Available from Acoustic Neuroma Association (ANA). 600 Peachtree Parkway, Suite 108, Cumming, GA 30041-8211. (770) 205-8211. Fax (770 www.ANAUSA.org. PRICE: \$2.00 plus shipping and handling.

Summary: This pamphlet includes an article originally published in the February 1994 issue of ANA Notes, a quarterly newsletter from the Acoustic Neuroma Association (ANA). Topics include the prevalence of headaches caused by Acoustic Neuroma; what the headaches are like; causes of the headaches, which include aseptic meningitis, coupling of the dura with neck muscles, nerve entrapment, low intracranial pressure, muscle spasms, and exacerbation of an underlying headache pattern; what can be done for these kind of headaches, which including drug therapy, surgery, local measures, and stress reduction; and prevention of post-surgery headaches. A collection of articles and letters from ANA members is included. Inside the back cover is a listing of ANA publications with pricing and shipping information.

#### The National Guideline Clearinghouse<sup>™</sup>

The National Guideline Clearinghouse<sup>™</sup> offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search this site located at **http://www.guideline.gov/** by using the keyword "headache" (or synonyms). The following was recently posted:

Source: American College of Radiology - Medical Specialty Society; 1996 (revised 1999); 7 pages

http://www.guideline.gov/summary/summary.aspx?doc\_id=2442&nbr=1668&string=headache

• Assessment: prevention of post-lumbar puncture headaches. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

Source: American Academy of Neurology - Medical Specialty Society; 2000 October; 6 pages

http://www.guideline.gov/summary/summary.aspx?doc\_id=2815&nbr=2041&string=headache

• Clinical policy: critical issues in the evaluation and management of patients presenting to the emergency department with acute headache

Source: American College of Emergency Physicians - Medical Specialty Society; 2002; 15 pages

http://www.guideline.gov/summary/summary.aspx?doc\_id=3298&nbr=2524&string=headache

#### • Diagnosis and management of headache

Source: National Committee on Neuroscience (Singapore) - National Government Agency [Non-U.S.]; 2000 November; 25 pages

http://www.guideline.gov/summary/summary.aspx?doc\_id=2838&nbr=2064&string=headache

#### • Migraine headache

Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1998 November (revised 2002 Jul); 74 pages

http://www.guideline.gov/summary/summary.aspx?doc\_id=3441&nbr=2667&a mp;string=headache

• Pharmacologic management of acute attacks of migraine and prevention of migraine headache

Source: American Academy of Family Physicians - Medical Specialty Society; 2002 November; 10 pages

http://www.guideline.gov/summary/summary.aspx?doc\_id=3592&nbr=2818&a mp;string=headache

• Practice parameter: evidence-based guidelines for migraine headache (an evidencebased review). Report of the Quality Standards Subcommittee of the American Academy of Neurology

Source: American Academy of Neurology - Medical Specialty Society; 2000 September; 10 pages

http://www.guideline.gov/summary/summary.aspx?doc\_id=2820&nbr=2046&string=headache

#### Healthfinder™

Healthfinder<sup>™</sup> 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:

#### • Cluster Headaches

Summary: A cluster headache is a rare type of headache that is more common in men. Cluster headaches start suddenly. The pain is usually behind or around one eye and is very severe.

Source: American Academy of Family Physicians

http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6312

#### Diseases & Conditions: Internet Resources for Alternative Medicine

Summary: Follow these links for information online related to alternative treatment options for this select group of diseases and disorders -- HIV/AIDS, asthma, cancer, epilepsy, headache, herpes, insomnia,

Source: Educational Institution -- Follow the Resource URL for More Information

http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=3983

#### Headache Information

Summary: A general overview of headache that includes a description of the disorder, and treatment, prognosis and research information.

Source: National Institute of Neurological Disorders and Stroke, National Institutes of Health

http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=780

#### • Headache Topics

Source: National Headache Foundation

http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6311

#### • Oooh, Your Aching Head

Summary: This fact sheet provides a definition of a headache to children including what causes a headache, different types of headaches and how to prevent headaches.

Source: Nemours Foundation

http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=4368

#### • Treating Insulin Reactions

Summary: Answers to questions about insulin reactions -- symptoms (shakiness, dizziness, sweating, hunger, headache, or sudden mood changes) and treatment.

Source: American Diabetes Association

http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=2218

#### 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 headache. 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<sup>®</sup>Health: http://my.webmd.com/health\_topics

#### Associations and Headache

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

• American Council for Headache Education

Telephone: (609) 423-0258 Toll-free: (800) 255-2243

Fax: (609) 423-0082

Email: achehq@talley.com

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

Background: The American Council for **Headache** Education (ACHE) is a national voluntary nonprofit organization dedicated to advancing the treatment and management of **headache** and to raising the public awareness of **headache** as a valid, biologically based illness. Established in 1989 and consisting of approximately 35,000 members, ACHE s educational mission reaches out to health career policy makers, employers, and opinion leaders as well as to affected individuals and their families. ACHE s goal is to help affected individuals gain more control over all aspects of their lives-medical, social, and economical. The organization offers a national network of **Headache** Support Groups; online networking opportunities and information via Prodigy, America Online, CompuServe, and the Internet; referrals; advocacy services;

and a variety of materials including local support group listings, brochures, booklets, and a regular newsletter entitled 'Headache.'.

Relevant area(s) of interest: Headaches

#### National Headache Foundation

Telephone: (312) 460-5399 Toll-free: (888) 643-5552

Fax: (312) 460-9049

Email: nhf1970@headaches.org

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

Background: Established in 1970, the National **Headache** Foundation is a not-for-profit organization dedicated to serving as an information resource to affected individuals, their families, and the physicians who treat them. The organization is also committed to promoting research into the causes of and treatments for **headaches** as well as increasing awareness among the public concerning the seriousness of **headaches** and the need for understanding and continuity of care for affected individuals. The National **Headache** Foundation funds ongoing medical research; sponsors public and professional education seminars across the country; and has a nationwide network of local support groups. In addition, the Foundation, which functions as a clearinghouse of information on **headaches**, provides a bimonthly newsletter, NHF Head Lines, brochures, and audiotapes and videotapes. Some materials are available in Spanish.

Relevant area(s) of interest: Headaches

## **Finding Associations**

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

#### 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 headache. 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 "headache" (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 "headache". 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 "headache" (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 "headache" (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.<sup>26</sup>

## 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

<sup>&</sup>lt;sup>26</sup> 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)<sup>27</sup>:

- 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.stmarysca.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/

<sup>&</sup>lt;sup>27</sup> Abstracted from http://www.nlm.nih.gov/medlineplus/libraries.html.

- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital, Waterbury), http://www.waterburyhospital.com/library/consumer.shtml
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute, Wilmington), http://www.christianacare.org/health\_guide/health\_guide\_pmri\_health\_info.cfm
- Delaware: Lewis B. Flinn Library (Delaware Academy of Medicine, Wilmington), http://www.delamed.org/chls.html
- **Georgia:** Family Resource Library (Medical College of Georgia, Augusta), http://cmc.mcg.edu/kids\_families/fam\_resources/fam\_res\_lib/frl.htm
- **Georgia:** Health Resource Center (Medical Center of Central Georgia, Macon), http://www.mccg.org/hrc/hrchome.asp
- Hawaii: Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library, Honolulu), http://hml.org/CHIS/
- Idaho: DeArmond Consumer Health Library (Kootenai Medical Center, Coeur d'Alene), http://www.nicon.org/DeArmond/index.htm
- Illinois: Health Learning Center of Northwestern Memorial Hospital (Chicago), http://www.nmh.org/health\_info/hlc.html
- Illinois: Medical Library (OSF Saint Francis Medical Center, Peoria), http://www.osfsaintfrancis.org/general/library/
- Kentucky: Medical Library Services for Patients, Families, Students & the Public (Central Baptist Hospital, Lexington), http://www.centralbap.com/education/community/library.cfm
- Kentucky: University of Kentucky Health Information Library (Chandler Medical Center, Lexington), http://www.mc.uky.edu/PatientEd/
- Louisiana: Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation, New Orleans), http://www.ochsner.org/library/
- Louisiana: Louisiana State University Health Sciences Center Medical Library-Shreveport, http://lib-sh.lsuhsc.edu/
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital, Farmington), http://www.fchn.org/fmh/lib.htm
- Maine: Gerrish-True Health Sciences Library (Central Maine Medical Center, Lewiston), http://www.cmmc.org/library/library.html
- Maine: Hadley Parrot Health Science Library (Eastern Maine Healthcare, Bangor), http://www.emh.org/hll/hpl/guide.htm
- Maine: Maine Medical Center Library (Maine Medical Center, Portland), http://www.mmc.org/library/
- Maine: Parkview Hospital (Brunswick), http://www.parkviewhospital.org/
- Maine: Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center, Biddeford), http://www.smmc.org/services/service.php3?choice=10
- **Maine:** Stephens Memorial Hospital's Health Information Library (Western Maine Health, Norway), http://www.wmhcc.org/Library/

- Manitoba, Canada: Consumer & Patient Health Information Service (University of Manitoba Libraries), http://www.umanitoba.ca/libraries/units/health/reference/chis.html
- Manitoba, Canada: J.W. Crane Memorial Library (Deer Lodge Centre, Winnipeg), http://www.deerlodge.mb.ca/crane\_library/about.asp
- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Dept. of Public Libraries, Wheaton Regional Library), http://www.mont.lib.md.us/healthinfo/hic.asp
- Massachusetts: Baystate Medical Center Library (Baystate Health System), http://www.baystatehealth.com/1024/
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), http://med-libwww.bu.edu/library/lib.html
- Massachusetts: Lowell General Hospital Health Sciences Library (Lowell General Hospital, Lowell), http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm
- Massachusetts: Paul E. Woodard Health Sciences Library (New England Baptist Hospital, Boston), http://www.nebh.org/health\_lib.asp
- Massachusetts: St. Luke's Hospital Health Sciences Library (St. Luke's Hospital, Southcoast Health System, New Bedford), http://www.southcoast.org/library/
- Massachusetts: Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), http://www.mgh.harvard.edu/library/chrcindex.html
- Massachusetts: UMass HealthNet (University of Massachusetts Medical School, Worchester), http://healthnet.umassmed.edu/
- Michigan: Botsford General Hospital Library Consumer Health (Botsford General Hospital, Library & Internet Services), http://www.botsfordlibrary.org/consumer.htm
- Michigan: Helen DeRoy Medical Library (Providence Hospital and Medical Centers), http://www.providence-hospital.org/library/
- Michigan: Marquette General Hospital Consumer Health Library (Marquette General Hospital, Health Information Center), http://www.mgh.org/center.html
- Michigan: Patient Education Resouce Center University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center, Ann Arbor), http://www.cancer.med.umich.edu/learn/leares.htm
- Michigan: Sladen Library & Center for Health Information Resources Consumer Health Information (Detroit), http://www.henryford.com/body.cfm?id=39330
- Montana: Center for Health Information (St. Patrick Hospital and Health Sciences Center, Missoula)
- National: Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), http://caphis.mlanet.org/directory/index.html
- **National:** National Network of Libraries of Medicine (National Library of Medicine) provides library services for health professionals in the United States who do not have access to a medical library, http://nnlm.gov/
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), http://nnlm.gov/members/

- Nevada: Health Science Library, West Charleston Library (Las Vegas-Clark County Library District, Las Vegas), http://www.lvccld.org/special\_collections/medical/index.htm
- New Hampshire: Dartmouth Biomedical Libraries (Dartmouth College Library, Hanover), http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/
- New Jersey: Consumer Health Library (Rahway Hospital, Rahway), http://www.rahwayhospital.com/library.htm
- New Jersey: Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center, Englewood), http://www.englewoodhospital.com/links/index.htm
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center, Englewood), http://www.geocities.com/ResearchTriangle/9360/
- New York: Choices in Health Information (New York Public Library) NLM Consumer Pilot Project participant, http://www.nypl.org/branch/health/links.html
- New York: Health Information Center (Upstate Medical University, State University of New York, Syracuse), http://www.upstate.edu/library/hic/
- New York: Health Sciences Library (Long Island Jewish Medical Center, New Hyde Park), http://www.lij.edu/library/library.html
- New York: ViaHealth Medical Library (Rochester General Hospital), http://www.nyam.org/library/
- Ohio: Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), http://www.akrongeneral.org/hwlibrary.htm
- **Oklahoma:** The Health Information Center at Saint Francis Hospital (Saint Francis Health System, Tulsa), http://www.sfh-tulsa.com/services/healthinfo.asp
- Oregon: Planetree Health Resource Center (Mid-Columbia Medical Center, The Dalles), http://www.mcmc.net/phrc/
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center, Hershey), http://www.hmc.psu.edu/commhealth/
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center, Danville), http://www.geisinger.edu/education/commlib.shtml
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital, Scranton), http://www.mth.org/healthwellness.html
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System, Pittsburgh), http://www.hsls.pitt.edu/guides/chi/hopwood/index\_html
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), http://www.collphyphil.org/kooppg1.shtml
- **Pennsylvania:** Learning Resources Center Medical Library (Susquehanna Health System, Williamsport), http://www.shscares.org/services/lrc/index.asp
- **Pennsylvania:** Medical Library (UPMC Health System, Pittsburgh), http://www.upmc.edu/passavant/library.htm
- Quebec, Canada: Medical Library (Montreal General Hospital), http://www.mghlib.mcgill.ca/

- **South Dakota:** Rapid City Regional Hospital Medical Library (Rapid City Regional Hospital), http://www.rcrh.org/Services/Library/Default.asp
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), http://hhw.library.tmc.edu/
- Washington: Community Health Library (Kittitas Valley Community Hospital), http://www.kvch.com/
- Washington: Southwest Washington Medical Center Library (Southwest Washington Medical Center, Vancouver), http://www.swmedicalcenter.com/body.cfm?id=72

# **ONLINE GLOSSARIES**

The Internet provides access to a number of free-to-use medical dictionaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: http://www.nlm.nih.gov/medlineplus/encyclopedia.html
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): http://www.medterms.com/Script/Main/hp.asp
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): http://www.intelihealth.com/IH/
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html
- On-line Medical Dictionary (CancerWEB): http://cancerweb.ncl.ac.uk/omd/
- Rare Diseases Terms (Office of Rare Diseases): http://ord.aspensys.com/asp/diseases/diseases.asp
- Technology Glossary (National Library of Medicine) Health Care Technology: http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm

Beyond these, MEDLINEplus contains a very patient-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia can be accessed at http://www.nlm.nih.gov/medlineplus/encyclopedia.html. ADAM is also available on commercial Web sites such as drkoop.com (http://www.drkoop.com/) and Web MD (http://my.webmd.com/adam/asset/adam\_disease\_articles/a\_to\_z/a). The NIH suggests the following Web sites in the ADAM Medical Encyclopedia when searching for information on headache:

• Basic Guidelines for Headache

#### Headache

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003024.htm

#### Headache causes

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002099.htm

• Signs & Symptoms for Headache

#### Blindness

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003040.htm

#### Coughing

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003072.htm

#### Depression

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003213.htm

#### Fatigue

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003088.htm

#### Fever

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003090.htm

#### Headache

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003024.htm

#### Headaches

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003024.htm

#### Impaired vision

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003029.htm

#### Muscle contraction

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003193.htm

#### Nasal discharge

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003051.htm

#### Nausea

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

#### Nausea and vomiting

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

#### Postnasal drip

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003051.htm

#### Sneezing

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003060.htm

#### Stiff neck

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003261.htm

#### Stress

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003211.htm

#### Tension

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003211.htm

## Vomiting

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

#### Weakness

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003174.htm

## Weight loss

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003107.htm

#### • Diagnostics and Tests for Headache

#### Biopsy

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003416.htm

#### Head CT scan

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003786.htm

#### Head MRI

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003791.htm

## Lumbar puncture

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003428.htm

#### Visual field

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003879.htm

#### • Nutrition for Headache

**Caffeine** Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002445.htm

#### • Background Topics for Headache

#### Aggravated by

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002227.htm

#### Head injury

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000028.htm

#### Pain medications

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002123.htm

#### Peripheral

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002273.htm

## Traumatic event

Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001924.htm

## **Online Dictionary Directories**

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical
- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): http://mel.lib.mi.us/health/health-dictionaries.html
- Patient Education: Glossaries (DMOZ Open Directory Project): http://dmoz.org/Health/Education/Patient\_Education/Glossaries/

270 Headache

 Web of Online Dictionaries (Bucknell University): http://www.yourdictionary.com/diction5.html#medicine

# HEADACHE DICTIONARY

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

5-Hydroxytryptophan: Precursor of serotonin used as antiepileptic and antidepressant. [NIH]

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]

Abdominal Cramps: Abdominal pain due to spasmodic contractions of the bowel. [NIH]

Abdominal Pain: Sensation of discomfort, distress, or agony in the abdominal region. [NIH]

**Abducens:** A striated, extrinsic muscle of the eyeball that originates from the annulus of Zinn. [NIH]

**Abducens Nerve:** The 6th cranial nerve. The abducens nerve originates in the abducens nucleus of the pons and sends motor fibers to the lateral rectus muscles of the eye. Damage to the nerve or its nucleus disrupts horizontal eye movement control. [NIH]

**Abducens Nerve Diseases:** Diseases of the sixth cranial (abducens) nerve or its nucleus in the pons. The nerve may be injured along its course in the pons, intracranially as it travels along the base of the brain, in the cavernous sinus, or at the level of superior orbital fissure or orbit. Dysfunction of the nerve causes lateral rectus muscle weakness, resulting in horizontal diplopia that is maximal when the affected eye is abducted and esotropia. Common conditions associated with nerve injury include intracranial hypertension; craniocerebral trauma; ischemia; and infratentorial neoplasms. [NIH]

Ablation: The removal of an organ by surgery. [NIH]

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

**Acculturation:** Process of cultural change in which one group or members of a group assimilates various cultural patterns from another. [NIH]

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

Acetone: A colorless liquid used as a solvent and an antiseptic. It is one of the ketone bodies produced during ketoacidosis. [NIH]

Acetylcholine: A neurotransmitter. Acetylcholine in vertebrates is the major transmitter at neuromuscular junctions, autonomic ganglia, parasympathetic effector junctions, a subset of sympathetic effector junctions, and at many sites in the central nervous system. It is generally not used as an administered drug because it is broken down very rapidly by cholinesterases, but it is useful in some ophthalmological applications. [NIH]

Acidosis: A pathologic condition resulting from accumulation of acid or depletion of the alkaline reserve (bicarbonate content) in the blood and body tissues, and characterized by an increase in hydrogen ion concentration. [EU]

Acne: A disorder of the skin marked by inflammation of oil glands and hair glands. [NIH]

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

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

Activities of Daily Living: The performance of the basic activities of self care, such as dressing, ambulation, eating, etc., in rehabilitation. [NIH]

Acuity: Clarity or clearness, especially of the vision. [EU]

Acupuncture Points: Designated locations along nerves or organ meridians for inserting acupuncture needles. [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]

Adenine: A purine base and a fundamental unit of adenine nucleotides. [NIH]

Adenocarcinoma: A malignant epithelial tumor with a glandular organization. [NIH]

Adenosine: A nucleoside that is composed of adenine and d-ribose. Adenosine or adenosine derivatives play many important biological roles in addition to being components of DNA and RNA. Adenosine itself is a neurotransmitter. [NIH]

Adenylate Cyclase: An enzyme of the lyase class that catalyzes the formation of cyclic AMP and pyrophosphate from ATP. EC 4.6.1.1. [NIH]

**Adipocytes:** Fat-storing cells found mostly in the abdominal cavity and subcutaneous tissue. Fat is usually stored in the form of tryglycerides. [NIH]

**Adjunctive Therapy:** Another treatment used together with the primary treatment. Its purpose is to assist the primary treatment. [NIH]

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

**Adjuvant:** A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

**Adjuvant Therapy:** Treatment given after the primary treatment to increase the chances of a cure. Adjuvant therapy may include chemotherapy, radiation therapy, or hormone therapy. [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]

Adrenal Glands: Paired glands situated in the retroperitoneal tissues at the superior pole of each kidney. [NIH]

Adrenal Medulla: The inner part of the adrenal gland; it synthesizes, stores and releases catecholamines. [NIH]

**Adrenergic:** Activated by, characteristic of, or secreting epinephrine or substances with similar activity; the term is applied to those nerve fibres that liberate norepinephrine at a synapse when a nerve impulse passes, i.e., the sympathetic fibres. [EU]

Adrenergic Antagonists: Drugs that bind to but do not activate adrenergic receptors.

Adrenergic antagonists block the actions of the endogenous adrenergic transmitters epinephrine and norepinephrine. [NIH]

Adrenergic Uptake Inhibitors: Drugs that block the transport of adrenergic transmitters into axon terminals or into storage vesicles within terminals. The tricyclic antidepressants (antidepressive agents, tricyclic) and amphetamines are among the therapeutically important drugs that may act via inhibition of adrenergic transport. Many of these drugs also block transport of serotonin. [NIH]

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

**Aerobic:** In biochemistry, reactions that need oxygen to happen or happen when oxygen is present. [NIH]

**Aerosol:** A solution of a drug which can be atomized into a fine mist for inhalation therapy. [EU]

**Afferent:** Concerned with the transmission of neural impulse toward the central part of the nervous system. [NIH]

Affinity: 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

**Agar:** A complex sulfated polymer of galactose units, extracted from Gelidium cartilagineum, Gracilaria confervoides, and related red algae. It is used as a gel in the preparation of solid culture media for microorganisms, as a bulk laxative, in making emulsions, and as a supporting medium for immunodiffusion and immunoelectrophoresis. [NIH]

**Age 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]

**Agonist:** In anatomy, a prime mover. In pharmacology, a drug that has affinity for and stimulates physiologic activity at cell receptors normally stimulated by naturally occurring substances. [EU]

Agoraphobia: Obsessive, persistent, intense fear of open places. [NIH]

**Agranulocytosis:** A decrease in the number of granulocytes (basophils, eosinophils, and neutrophils). [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]

**Akathisia:** 1. A condition of motor restlessness in which there is a feeling of muscular quivering, an urge to move about constantly, and an inability to sit still, a common extrapyramidal side effect of neuroleptic drugs. 2. An inability to sit down because of intense anxiety at the thought of doing so. [EU]

Alendronate: A nonhormonal medication for the treatment of postmenopausal osteoporosis in women. This drug builds healthy bone, restoring some of the bone loss as a result of osteoporosis. [NIH]

**Alertness:** A state of readiness to detect and respond to certain specified small changes occurring at random intervals in the environment. [NIH]

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

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

Alimentary: Pertaining to food or nutritive material, or to the organs of digestion. [EU]

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

**Alkaloid:** A member of a large group of chemicals that are made by plants and have nitrogen in them. Some alkaloids have been shown to work against cancer. [NIH]

Allergen: An antigenic substance capable of producing immediate-type hypersensitivity (allergy). [EU]

Allergic Rhinitis: Inflammation of the nasal mucous membrane associated with hay fever; fits may be provoked by substances in the working environment. [NIH]

**Alpha Particles:** Positively charged particles composed of two protons and two neutrons, i.e., helium nuclei, emitted during disintegration of very heavy isotopes; a beam of alpha particles or an alpha ray has very strong ionizing power, but weak penetrability. [NIH]

**Alpha-1:** A protein with the property of inactivating proteolytic enzymes such as leucocyte collagenase and elastase. [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]

Alternative Splicing: A process whereby multiple protein isoforms are generated from a single gene. Alternative splicing involves the splicing together of nonconsecutive exons during the processing of some, but not all, transcripts of the gene. Thus a particular exon may be connected to any one of several alternative exons to form messenger RNA. The alternative forms produce proteins in which one part is common while the other part is different. [NIH]

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

Amenorrhea: Absence of menstruation. [NIH]

**Amine:** An organic compound containing nitrogen; any member of a group of chemical compounds formed from ammonia by replacement of one or more of the hydrogen atoms by organic (hydrocarbon) radicals. The amines are distinguished as primary, secondary, and tertiary, according to whether one, two, or three hydrogen atoms are replaced. The amines include allylamine, amylamine, ethylamine, methylamine, phenylamine, propylamine, and many other compounds. [EU]

**Amino Acid Sequence:** The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

**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]

**Aminopropionitrile:** 3-Aminopropanenitrile. Reagent used as an intermediate in the manufacture of beta-alanine and pantothenic acid. [NIH]

**Amitriptyline:** Tricyclic antidepressant with anticholinergic and sedative properties. It appears to prevent the re-uptake of norepinephrine and serotonin at nerve terminals, thus potentiating the action of these neurotransmitters. Amitriptyline also appears to antaganize cholinergic and alpha-1 adrenergic responses to bioactive amines. [NIH]

**Amphetamines:** Analogs or derivatives of amphetamine. Many are sympathomimetics and central nervous system stimulators causing excitation, vasopression, bronchodilation, and to varying degrees, anorexia, analepsis, nasal decongestion, and some smooth muscle relaxation. [NIH]

**Amyloid:** A general term for a variety of different proteins that accumulate as extracellular fibrils of 7-10 nm and have common structural features, including a beta-pleated sheet conformation and the ability to bind such dyes as Congo red and thioflavine (Kandel, Schwartz, and Jessel, Principles of Neural Science, 3rd ed). [NIH]

**Anaesthesia:** Loss of feeling or sensation. Although the term is used for loss of tactile sensibility, or of any of the other senses, it is applied especially to loss of the sensation of pain, as it is induced to permit performance of surgery or other painful procedures. [EU]

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

Anal Fissure: A small tear in the anus that may cause itching, pain, or bleeding. [NIH]

**Analeptic:** A drug which acts as a restorative, such as caffeine, amphetamine, pentylenetetrazol, etc. [EU]

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

Analog: In chemistry, a substance that is similar, but not identical, to another. [NIH]

Anaphylactic: Pertaining to anaphylaxis. [EU]

**Anaphylatoxins:** The family of peptides C3a, C4a, C5a, and C5a des-arginine produced in the serum during complement activation. They produce smooth muscle contraction, mast cell histamine release, affect platelet aggregation, and act as mediators of the local inflammatory process. The order of anaphylatoxin activity from strongest to weakest is C5a, C3a, C4a, and C5a des-arginine. The latter is the so-called "classical" anaphylatoxin but shows no spasmogenic activity though it contains some chemotactic ability. [NIH]

**Anaphylaxis:** An acute hypersensitivity reaction due to exposure to a previously encountered antigen. The reaction may include rapidly progressing urticaria, respiratory distress, vascular collapse, systemic shock, and death. [NIH]

Anatomical: Pertaining to anatomy, or to the structure of the organism. [EU]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

**Anesthesia:** A state characterized by loss of feeling or sensation. This depression of nerve function is usually the result of pharmacologic action and is induced to allow performance of surgery or other painful procedures. [NIH]

**Anesthetics:** Agents that are capable of inducing a total or partial loss of sensation, especially tactile sensation and pain. They may act to induce general anesthesia, in which an unconscious state is achieved, or may act locally to induce numbness or lack of sensation at

a targeted site. [NIH]

Aneurysm: A sac formed by the dilatation of the wall of an artery, a vein, or the heart. [NIH]

Angina: Chest pain that originates in the heart. [NIH]

**Angina Pectoris:** The symptom of paroxysmal pain consequent to myocardial ischemia usually of distinctive character, location and radiation, and provoked by a transient stressful situation during which the oxygen requirements of the myocardium exceed the capacity of the coronary circulation to supply it. [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]

Angioma: A tumor composed of lymphatic or blood vessels. [NIH]

**Angiotensinogen:** An alpha-globulin of which a fragment of 14 amino acids is converted by renin to angiotensin I, the inactive precursor of angiotensin II. It is a member of the serpin superfamily. [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]

Ankle: That part of the lower limb directly above the foot. [NIH]

Anomalies: Birth defects; abnormalities. [NIH]

**Anorexia:** Lack or loss of appetite for food. Appetite is psychologic, dependent on memory and associations. Anorexia can be brought about by unattractive food, surroundings, or company. [NIH]

**Anorexia Nervosa:** The chief symptoms are inability to eat, weight loss, and amenorrhea. [NIH]

**Anoxia:** Clinical manifestation of respiratory distress consisting of a relatively complete absence of oxygen. [NIH]

**Antagonism:** Interference with, or inhibition of, the growth of a living organism by another living organism, due either to creation of unfavorable conditions (e. g. exhaustion of food supplies) or to production of a specific antibiotic substance (e. g. penicillin). [NIH]

**Antecedent:** Existing or occurring before in time or order often with consequential effects. [EU]

**Anterior Cerebral Artery:** Artery formed by the bifurcation of the internal carotid artery. Branches of the anterior cerebral artery supply the caudate nucleus, internal capsule, putamen, septal nuclei, gyrus cinguli, and surfaces of the frontal lobe and parietal lobe. [NIH]

**Antibacterial:** A substance that destroys bacteria or suppresses their growth or reproduction. [EU]

**Antibiotic:** A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

**Antibodies:** Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the antigen that induced their synthesis in cells of the lymphoid series (especially plasma cells), or with an antigen closely related to it. [NIH]

**Antibody:** A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier

for white blood cells to destroy the antigen. [NIH]

**Anticholinergic:** An agent that blocks the parasympathetic nerves. Called also parasympatholytic. [EU]

**Anticoagulant:** A drug that helps prevent blood clots from forming. Also called a blood thinner. [NIH]

Anticonvulsants: Drugs used to prevent seizures or reduce their severity. [NIH]

Antidepressant: A drug used to treat depression. [NIH]

**Antiemetic:** An agent that prevents or alleviates nausea and vomiting. Also antinauseant. [EU]

Antiepileptic: An agent that combats epilepsy. [EU]

**Antifungal:** Destructive to fungi, or suppressing their reproduction or growth; effective against fungal infections. [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]

**Antigen-Antibody Complex:** The complex formed by the binding of antigen and antibody molecules. The deposition of large antigen-antibody complexes leading to tissue damage causes immune complex diseases. [NIH]

**Antihistamine:** A drug that counteracts the action of histamine. The antihistamines are of two types. The conventional ones, as those used in allergies, block the H1 histamine receptors, whereas the others block the H2 receptors. Called also antihistaminic. [EU]

Anti-infective: An agent that so acts. [EU]

Anti-inflammatory: Having to do with reducing inflammation. [NIH]

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

Antimicrobial: Killing microorganisms, or suppressing their multiplication or growth. [EU]

Antipsychotic: Effective in the treatment of psychosis. Antipsychotic drugs (called also neuroleptic drugs and major tranquilizers) are a chemically diverse (including phenothiazines, thioxanthenes, butyrophenones, dibenzoxazepines, dibenzodiazepines, and diphenylbutylpiperidines) but pharmacologically similar class of drugs used to treat schizophrenic, paranoid, schizoaffective, and other psychotic disorders; acute delirium and dementia, and manic episodes (during induction of lithium therapy); to control the movement disorders associated with Huntington's chorea, Gilles de la Tourette's syndrome, and ballismus; and to treat intractable hiccups and severe nausea and vomiting. Antipsychotic agents bind to dopamine, histamine, muscarinic cholinergic, a-adrenergic, and serotonin receptors. Blockade of dopaminergic transmission in various areas is thought to be responsible for their major effects : antipsychotic action by blockade in the mesolimbic and mesocortical areas; extrapyramidal side effects (dystonia, akathisia, parkinsonism, and tardive dyskinesia) by blockade in the basal ganglia; and antiemetic effects by blockade in the chemoreceptor trigger zone of the medulla. Sedation and autonomic side effects (orthostatic hypotension, blurred vision, dry mouth, nasal congestion and constipation) are caused by blockade of histamine, cholinergic, and adrenergic receptors. [EU]

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

**Antiseptic:** A substance that inhibits the growth and development of microorganisms without necessarily killing them. [EU]

Antitussive: An agent that relieves or prevents cough. [EU]

Antiviral: Destroying viruses or suppressing their replication. [EU]

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

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

**Anxiety Disorders:** Disorders in which anxiety (persistent feelings of apprehension, tension, or uneasiness) is the predominant disturbance. [NIH]

Apathy: Lack of feeling or emotion; indifference. [EU]

Aperture: A natural hole of perforation, especially one in a bone. [NIH]

Apnoea: Cessation of breathing. [EU]

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

Aqueous: Having to do with water. [NIH]

**Arachidonate 12-Lipoxygenase:** An enzyme that catalyzes the oxidation of arachidonic acid to yield 12-hydroperoxyarachidonate (12-HPETE) which is itself rapidly converted by a peroxidase to 12-hydroxy-5,8,10,14-eicosatetraenoate (12-HETE). The 12-hydroperoxides are preferentially formed in platelets. EC 1.13.11.31. [NIH]

**Arachidonate 15-Lipoxygenase:** An enzyme that catalyzes the oxidation of arachidonic acid to yield 15-hydroperoxyarachidonate (15-HPETE) which is rapidly converted to 15-hydroxy-5,8,11,13-eicosatetraenoate (15-HETE). The 15-hydroperoxides are preferentially formed in neutrophils and lymphocytes. EC 1.13.11.33. [NIH]

**Arachidonate Lipoxygenases:** Enzymes catalyzing the oxidation of arachidonic acid to hydroperoxyarachidonates (HPETES). These products are then rapidly converted by a peroxidase to hydroxyeicosatetraenoic acids (HETES). The positional specificity of the enzyme reaction varies from tissue to tissue. The final lipoxygenase pathway leads to the leukotrienes. EC 1.13.11.-. [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]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Aromatic: Having a spicy odour. [EU]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arteriolar: Pertaining to or resembling arterioles. [EU]

**Arterioles:** The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

**Arteriolosclerosis:** Sclerosis and thickening of the walls of the smaller arteries (arterioles). Hyaline arteriolosclerosis, in which there is homogeneous pink hyaline thickening of the arteriolar walls, is associated with benign nephrosclerosis. Hyperplastic arteriolosclerosis, in which there is a concentric thickening with progressive narrowing of the lumina may be associated with malignant hypertension, nephrosclerosis, and scleroderma. [EU]

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]

Arteritis: Inflammation of an artery. [NIH]

Arthralgia: Pain in the joint. [NIH]

Arthrosis: A disease of a joint. [EU]

Articular: Of or pertaining to a joint. [EU]

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

**Aspartame:** Flavoring agent sweeter than sugar, metabolized as phenylalanine and aspartic acid. [NIH]

Aspartate: A synthetic amino acid. [NIH]

**Aspartic:** The naturally occurring substance is L-aspartic acid. One of the acidic-amino-acids is obtained by the hydrolysis of proteins. [NIH]

Aspartic Acid: One of the non-essential amino acids commonly occurring in the L-form. It is found in animals and plants, especially in sugar cane and sugar beets. It may be a neurotransmitter. [NIH]

**Asphyxia:** A pathological condition caused by lack of oxygen, manifested in impending or actual cessation of life. [NIH]

**Aspirin:** A drug that reduces pain, fever, inflammation, and blood clotting. Aspirin belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is also being studied in cancer prevention. [NIH]

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

**Astemizole:** A long-acting, non-sedative antihistaminic used in the treatment of seasonal allergic rhinitis, asthma, allergic conjunctivitis, and chronic idiopathic urticaria. The drug is well tolerated and has no anticholinergic side effects. [NIH]

**Asthenia:** Clinical sign or symptom manifested as debility, or lack or loss of strength and energy. [NIH]

**Asthenopia:** Term generally used to describe complaints related to refractive error, ocular muscle imbalance, including pain or aching around the eyes, burning and itchiness of the eyelids, ocular fatigue, and headaches. [NIH]

**Astringents:** Agents, usually topical, that cause the contraction of tissues for the control of bleeding or secretions. [NIH]

Astrocytes: The largest and most numerous neuroglial cells in the brain and spinal cord. Astrocytes (from "star" cells) are irregularly shaped with many long processes, including those with "end feet" which form the glial (limiting) membrane and directly and indirectly contribute to the blood brain barrier. They regulate the extracellular ionic and chemical environment, and "reactive astrocytes" (along with microglia) respond to injury. Astrocytes have high- affinity transmitter uptake systems, voltage-dependent and transmitter-gated ion channels, and can release transmitter, but their role in signaling (as in many other functions) is not well understood. [NIH]

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Asynchronous: Pacing mode where only one timing interval exists, that between the stimuli.
While the duration of this interval may be varied, it is not modified by any sensed event once set. As no sensing occurs, the upper and lower rate intervals are the same as the pacema. [NIH]

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]

Atopic: Pertaining to an atopen or to atopy; allergic. [EU]

Atrial: Pertaining to an atrium. [EU]

Atrioventricular: Pertaining to an atrium of the heart and to a ventricle. [EU]

**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]

**Atrophy:** Decrease in the size of a cell, tissue, organ, or multiple organs, associated with a variety of pathological conditions such as abnormal cellular changes, ischemia, malnutrition, or hormonal changes. [NIH]

Attenuated: Strain with weakened or reduced virulence. [NIH]

Attenuation: Reduction of transmitted sound energy or its electrical equivalent. [NIH]

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

**Aura:** A subjective sensation or motor phenomenon that precedes and marks the of a paroxysmal attack, such as an epileptic attack on set. [EU]

Aural: Pertaining to or perceived by the ear, as an aural stimulus. [EU]

Auricular: Pertaining to an auricle or to the ear, and, formerly, to an atrium of the heart. [EU]

**Autacoids:** A chemically diverse group of substances produced by various tissues in the body that cause slow contraction of smooth muscle; they have other intense but varied pharmacologic activities. [NIH]

**Autoantibodies:** Antibodies that react with self-antigens (autoantigens) of the organism that produced them. [NIH]

**Autodigestion:** Autolysis; a condition found in disease of the stomach: the stomach wall is digested by the gastric juice. [NIH]

**Autogenic:** A type of succession when the developing vegetation itself is the cause for the succession. [NIH]

**Autogenic Training:** Technique based on muscle relaxation during self-hypnotic exercises. It is used in conjunction with psychotherapy. [NIH]

Autoimmune disease: A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. [NIH]

Autonomic: Self-controlling; functionally independent. [EU]

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

**Axons:** Nerve fibers that are capable of rapidly conducting impulses away from the neuron cell body. [NIH]

**Azithromycin:** A semi-synthetic macrolide antibiotic structurally related to erythromycin. It has been used in the treatment of Mycobacterium avium intracellulare infections,

toxoplasmosis, and cryptosporidiosis. [NIH]

**Back Pain:** Acute or chronic pain located in the posterior regions of the trunk, including the thoracic, lumbar, sacral, or adjacent regions. [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]

**Barbiturates:** A class of chemicals derived from barbituric acid or thiobarbituric acid. Many of these are medically important as sedatives and hypnotics (sedatives, barbiturate), as anesthetics, or as anticonvulsants. [NIH]

**Baroreflex:** A negative feedback system which buffers short-term changes in blood pressure. Increased pressure stretches blood vessels which activates pressoreceptors (baroreceptors) in the vessel walls. The net response of the central nervous system is a reduction of central sympathetic outflow. This reduces blood pressure both by decreasing peripheral vascular resistance and by lowering cardiac output. Because the baroreceptors are tonically active, the baroreflex can compensate rapidly for both increases and decreases in blood pressure. [NIH]

**Basal Ganglia:** Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [NIH]

**Basal Ganglia Diseases:** Diseases of the basal ganglia including the putamen; globus pallidus; claustrum; amygdala; and caudate nucleus. Dyskinesias (most notably involuntary movements and alterations of the rate of movement) represent the primary clinical manifestations of these disorders. Common etiologies include cerebrovascular disease; neurodegenerative diseases; and craniocerebral trauma. [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]

**Basophils:** Granular leukocytes characterized by a relatively pale-staining, lobate nucleus and cytoplasm containing coarse dark-staining granules of variable size and stainable by basic dyes. [NIH]

Bed Rest: Confinement of an individual to bed for therapeutic or experimental reasons. [NIH]

**Benign:** Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Benign prostatic hyperplasia: A benign (noncancerous) condition in which an overgrowth

of prostate tissue pushes against the urethra and the bladder, blocking the flow of urine. Also called benign prostatic hypertrophy or BPH. [NIH]

**Benzene:** Toxic, volatile, flammable liquid hydrocarbon biproduct of coal distillation. It is used as an industrial solvent in paints, varnishes, lacquer thinners, gasoline, etc. Benzene causes central nervous system damage acutely and bone marrow damage chronically and is carcinogenic. It was formerly used as parasiticide. [NIH]

**Benzodiazepines:** A two-ring heterocyclic compound consisting of a benzene ring fused to a diazepine ring. Permitted is any degree of hydrogenation, any substituents and any H-isomer. [NIH]

**Beta blocker:** A drug used to slow the heart rate and reduce pressure inside blood vessels. It also can regulate heart rhythm. [NIH]

Beta-pleated: Particular three-dimensional pattern of amyloidoses. [NIH]

Bewilderment: Impairment or loss of will power. [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]

Biliary: Having to do with the liver, bile ducts, and/or gallbladder. [NIH]

Biliary Tract: The gallbladder and its ducts. [NIH]

**Bioavailability:** The degree to which a drug or other substance becomes available to the target tissue after administration. [EU]

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

**Biological response modifier:** BRM. A substance that stimulates the body's response to infection and disease. [NIH]

**Biological therapy:** Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier (BRM) therapy. [NIH]

**Bioluminescence:** The emission of light by living organisms such as the firefly, certain mollusks, beetles, fish, bacteria, fungi and protozoa. [NIH]

**Biomarkers:** Substances sometimes found in an increased amount in the blood, other body fluids, or tissues and that may suggest the presence of some types of cancer. Biomarkers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and GI tract cancers), and PSA (prostate cancer). Also called tumor markers. [NIH]

**Biopsy:** Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

**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]

**Bipolar Disorder:** A major affective disorder marked by severe mood swings (manic or major depressive episodes) and a tendency to remission and recurrence. [NIH]

**Bladder:** The organ that stores urine. [NIH]

**Blastocyst:** The mammalian embryo in the post-morula stage in which a fluid-filled cavity, enclosed primarily by trophoblast, contains an inner cell mass which becomes the embryonic disc. [NIH]

**Blepharospasm:** Excessive winking; tonic or clonic spasm of the orbicularis oculi muscle. [NIH]

Bloating: Fullness or swelling in the abdomen that often occurs after meals. [NIH]

**Blood Coagulation:** The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [NIH]

**Blood Flow Velocity:** A value equal to the total volume flow divided by the cross-sectional area of the vascular bed. [NIH]

Blood Glucose: Glucose in blood. [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 pressure:** The pressure of blood against the walls of a blood vessel or heart chamber. Unless there is reference to another location, such as the pulmonary artery or one of the heart chambers, it refers to the pressure in the systemic arteries, as measured, for example, in the forearm. [NIH]

**Blood vessel:** A tube in the body through which blood circulates. Blood vessels include a network of arteries, arterioles, capillaries, venules, and veins. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Body Regions: Anatomical areas of the body. [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 metastases:** Cancer that has spread from the original (primary) tumor to the bone. [NIH]

**Bone scan:** A technique to create images of bones on a computer screen or on film. A small amount of radioactive material is injected into a blood vessel and travels through the bloodstream; it collects in the bones and is detected by a scanner. [NIH]

**Botulinum Toxins:** Toxins produced by Clostridium botulinum. There are at least seven different substances, most being proteins. They have neuro-, entero-, and hemotoxic properties, are immunogenic, and include the most potent poisons known. The most commonly used apparently blocks release of acetylcholine at cholinergic synapses. [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]

**Brachial Artery:** The continuation of the axillary artery; it branches into the radial and ulnar arteries. [NIH]

**Brachial Plexus:** The large network of nerve fibers which distributes the innervation of the upper extremity. The brachial plexus extends from the neck into the axilla. In humans, the nerves of the plexus usually originate from the lower cervical and the first thoracic spinal cord segments (C5-C8 and T1), but variations are not uncommon. [NIH]

**Bradykinin:** A nonapeptide messenger that is enzymatically produced from kallidin in the blood where it is a potent but short-lived agent of arteriolar dilation and increased capillary permeability. Bradykinin is also released from mast cells during asthma attacks, from gut walls as a gastrointestinal vasodilator, from damaged tissues as a pain signal, and may be a neurotransmitter. [NIH]

**Brain Infarction:** The formation of an area of necrosis in the brain, including the cerebral hemispheres (cerebral infarction), thalami, basal ganglia, brain stem (brain stem infarctions), or cerebellum secondary to an insufficiency of arterial or venous blood flow. [NIH]

**Brain Ischemia:** Localized reduction of blood flow to brain tissue due to arterial obtruction or systemic hypoperfusion. This frequently occurs in conjuction with brain hypoxia. Prolonged ischemia is associated with brain infarction. [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]

**Brain Stem:** The part of the brain that connects the cerebral hemispheres with the spinal cord. It consists of the mesencephalon, pons, and medulla oblongata. [NIH]

**Brain Stem Infarctions:** Infarctions that occur in the brain stem which is comprised of the midbrain, pons, and medulla. There are several named syndromes characterized by their distinctive clinical manifestations and specific sites of ischemic injury. [NIH]

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

Breakdown: A physical, metal, or nervous collapse. [NIH]

**Bromelain:** An enzyme found in pineapples that breaks down other proteins, such as collagen and muscle fiber, and has anti-inflammatory properties. It is used as a meat tenderizer in the food industry. [NIH]

**Bromine:** A halogen with the atomic symbol Br, atomic number 36, and atomic weight 79.904. It is a volatile reddish-brown liquid that gives off suffocating vapors, is corrosive to the skin, and may cause severe gastroenteritis if ingested. [NIH]

**Bronchi:** The larger air passages of the lungs arising from the terminal bifurcation of the trachea. [NIH]

Bronchial: Pertaining to one or more bronchi. [EU]

**Bronchial Hyperreactivity:** Tendency of the smooth muscle of the tracheobronchial tree to contract more intensely in response to a given stimulus than it does in the response seen in normal individuals. This condition is present in virtually all symptomatic patients with asthma. The most prominent manifestation of this smooth muscle contraction is a decrease in airway caliber that can be readily measured in the pulmonary function laboratory. [NIH]

Bronchitis: Inflammation (swelling and reddening) of the bronchi. [NIH]

Bruxism: A disorder characterized by grinding and clenching of the teeth. [NIH]

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

**Buffers:** A chemical system that functions to control the levels of specific ions in solution. When the level of hydrogen ion in solution is controlled the system is called a pH buffer. [NIH]

Bulimia: Episodic binge eating. The episodes may be associated with the fear of not being

able to stop eating, depressed mood, or self-deprecating thoughts (binge-eating disorder) and may frequently be terminated by self-induced vomiting (bulimia nervosa). [NIH]

Bullous: Pertaining to or characterized by bullae. [EU]

**Burns:** Injuries to tissues caused by contact with heat, steam, chemicals (burns, chemical), electricity (burns, electric), or the like. [NIH]

**Burns, Electric:** Burns produced by contact with electric current or from a sudden discharge of electricity. [NIH]

**Caffeine:** A methylxanthine naturally occurring in some beverages and also used as a pharmacological agent. Caffeine's most notable pharmacological effect is as a central nervous system stimulant, increasing alertness and producing agitation. It also relaxes smooth muscle, stimulates cardiac muscle, stimulates diuresis, and appears to be useful in the treatment of some types of headache. Several cellular actions of caffeine have been observed, but it is not entirely clear how each contributes to its pharmacological profile. Among the most important are inhibition of cyclic nucleotide phosphodiesterases, antagonism of adenosine receptors, and modulation of intracellular calcium handling. [NIH]

**Calcification:** Deposits of calcium in the tissues of the breast. Calcification in the breast can be seen on a mammogram, but cannot be detected by touch. There are two types of breast calcification, macrocalcification and microcalcification. Macrocalcifications are large deposits and are usually not related to cancer. Microcalcifications are specks of calcium that may be found in an area of rapidly dividing cells. Many microcalcifications clustered together may be a sign of cancer. [NIH]

**Calcitonin Gene-Related Peptide:** Calcitonin gene-related peptide. A 37-amino acid peptide derived from the calcitonin gene. It occurs as a result of alternative processing of mRNA from the calcitonin gene. The neuropeptide is widely distributed in neural tissue of the brain, gut, perivascular nerves, and other tissue. The peptide produces multiple biological effects and has both circulatory and neurotransmitter modes of action. In particular, it is a potent endogenous vasodilator. [NIH]

**Calcium:** A basic element found in nearly all organized tissues. It is a member of the alkaline earth family of metals with the atomic symbol Ca, atomic number 20, and atomic weight 40. Calcium is the most abundant mineral in the body and combines with phosphorus to form calcium phosphate in the bones and teeth. It is essential for the normal functioning of nerves and muscles and plays a role in blood coagulation (as factor IV) and in many enzymatic processes. [NIH]

**Calcium channel blocker:** A drug used to relax the blood vessel and heart muscle, causing pressure inside blood vessels to drop. It also can regulate heart rhythm. [NIH]

**Calcium Channel Blockers:** A class of drugs that act by selective inhibition of calcium influx through cell membranes or on the release and binding of calcium in intracellular pools. Since they are inducers of vascular and other smooth muscle relaxation, they are used in the drug therapy of hypertension and cerebrovascular spasms, as myocardial protective agents, and in the relaxation of uterine spasms. [NIH]

**Calcium Channels:** Voltage-dependent cell membrane glycoproteins selectively permeable to calcium ions. They are categorized as L-, T-, N-, P-, Q-, and R-types based on the activation and inactivation kinetics, ion specificity, and sensitivity to drugs and toxins. The L- and T-types are present throughout the cardiovascular and central nervous systems and the N-, P-, Q-, & R-types are located in neuronal tissue. [NIH]

**Calcium Signaling:** Signal transduction mechanisms whereby calcium mobilization (from outside the cell or from intracellular storage pools) to the cytoplasm is triggered by external stimuli. Calcium signals are often seen to propagate as waves, oscillations, spikes or puffs.

The calcium acts as an intracellular messenger by activating calcium-responsive proteins. [NIH]

**Calculi:** An abnormal concretion occurring mostly in the urinary and biliary tracts, usually composed of mineral salts. Also called stones. [NIH]

**Calmodulin:** A heat-stable, low-molecular-weight activator protein found mainly in the brain and heart. The binding of calcium ions to this protein allows this protein to bind to cyclic nucleotide phosphodiesterases and to adenyl cyclase with subsequent activation. Thereby this protein modulates cyclic AMP and cyclic GMP levels. [NIH]

**Candidiasis:** Infection with a fungus of the genus Candida. It is usually a superficial infection of the moist cutaneous areas of the body, and is generally caused by C. albicans; it most commonly involves the skin (dermatocandidiasis), oral mucous membranes (thrush, def. 1), respiratory tract (bronchocandidiasis), and vagina (vaginitis). Rarely there is a systemic infection or endocarditis. Called also moniliasis, candidosis, oidiomycosis, and formerly blastodendriosis. [EU]

**Candidosis:** An infection caused by an opportunistic yeasts that tends to proliferate and become pathologic when the environment is favorable and the host resistance is weakened. [NIH]

**Capillary:** Any one of the minute vessels that connect the arterioles and venules, forming a network in nearly all parts of the body. Their walls act as semipermeable membranes for the interchange of various substances, including fluids, between the blood and tissue fluid; called also vas capillare. [EU]

**Capsaicin:** Cytotoxic alkaloid from various species of Capsicum (pepper, paprika), of the Solanaceae. [NIH]

**Capsicum:** A genus of Solanaceous shrubs that yield capsaicin. Several varieties have sweet or pungent edible fruits that are used as vegetables when fresh and spices when the pods are dried. [NIH]

Capsular: Cataract which is initiated by an opacification at the surface of the lens. [NIH]

Capsules: Hard or soft soluble containers used for the oral administration of medicine. [NIH]

**Carbohydrates:** The largest class of organic compounds, including starches, glycogens, cellulose, gums, and simple sugars. Carbohydrates are composed of carbon, hydrogen, and oxygen in a ratio of Cn(H2O)n. [NIH]

**Carbon Dioxide:** A colorless, odorless gas that can be formed by the body and is necessary for the respiration cycle of plants and animals. [NIH]

Carboxy: Cannabinoid. [NIH]

Carcinogenic: Producing carcinoma. [EU]

**Carcinogens:** Substances that increase the risk of neoplasms in humans or animals. Both genotoxic chemicals, which affect DNA directly, and nongenotoxic chemicals, which induce neoplasms by other mechanism, are included. [NIH]

**Carcinoid:** A type of tumor usually found in the gastrointestinal system (most often in the appendix), and sometimes in the lungs or other sites. Carcinoid tumors are usually benign. [NIH]

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

Cardiac arrest: A sudden stop of heart function. [NIH]

**Cardiac Output:** The volume of blood passing through the heart per unit of time. It is usually expressed as liters (volume) per minute so as not to be confused with stroke volume (volume per beat). [NIH]

**Cardiomyopathy:** A general diagnostic term designating primary myocardial disease, often of obscure or unknown etiology. [EU]

Cardioselective: Having greater activity on heart tissue than on other tissue. [EU]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

**Cardiovascular disease:** Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

**Carotene:** The general name for a group of pigments found in green, yellow, and leafy vegetables, and yellow fruits. The pigments are fat-soluble, unsaturated aliphatic hydrocarbons functioning as provitamins and are converted to vitamin A through enzymatic processes in the intestinal wall. [NIH]

**Carpal Tunnel Syndrome:** A median nerve injury inside the carpal tunnel that results in symptoms of pain, numbness, tingling, clumsiness, and a lack of sweating, which can be caused by work with certain hand and wrist postures. [NIH]

**Case report:** A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

**Case series:** A group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information (for example, age, gender, ethnic origin) and information on diagnosis, treatment, response to treatment, and follow-up after treatment. [NIH]

**Catecholamine:** A group of chemical substances manufactured by the adrenal medulla and secreted during physiological stress. [NIH]

**Catheterization:** Use or insertion of a tubular device into a duct, blood vessel, hollow organ, or body cavity for injecting or withdrawing fluids for diagnostic or therapeutic purposes. It differs from intubation in that the tube here is used to restore or maintain patency in obstructions. [NIH]

**Cauda Equina:** The lower part of the spinal cord consisting of the lumbar, sacral, and coccygeal nerve roots. [NIH]

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

Caudalis: Brain region that controls singing processes. [NIH]

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 Count:** A count of the number of cells of a specific kind, usually measured per unit volume of sample. [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 Degranulation:** The process of losing secretory granules (secretory vesicles). This occurs, for example, in mast cells, basophils, neutrophils, eosinophils, and platelets when secretory products are released from the granules by exocytosis. [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 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 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]

**Cellulose:** A polysaccharide with glucose units linked as in cellobiose. It is the chief constituent of plant fibers, cotton being the purest natural form of the substance. As a raw material, it forms the basis for many derivatives used in chromatography, ion exchange materials, explosives manufacturing, and pharmaceutical preparations. [NIH]

**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]

**Cerebellopontine:** Going from the cerebellum (the part of the brain responsible for coordinating movement) to the pons (part of the central nervous system located near the base of the brain.) [NIH]

Cerebellopontine Angle: Junction between the cerebellum and the pons. [NIH]

**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 Aqueduct:** Narrow channel in the mesencephalon that connects the third and fourth ventricles. [NIH]

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

**Cerebral hemispheres:** The two halves of the cerebrum, the part of the brain that controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. The right hemisphere controls muscle movement on the left side of the body, and the left hemisphere controls muscle movement on the right side of the body. [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]

Cerebral Palsy: Refers to a motor disability caused by a brain dysfunction. [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]

**Cerebrospinal Fluid Pressure:** Manometric pressure of the cerebrospinal fluid as measured by lumbar, cerebroventricular, or cisternal puncture. Within the cranial cavity it is called intracranial pressure. [NIH]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

**Cerebrovascular Disorders:** A broad category of disorders characterized by impairment of blood flow in the arteries and veins which supply the brain. These include cerebral infarction; brain ischemia; hypoxia, brain; intracranial embolism and thrombosis; intracranial arteriovenous malformations; and vasculitis, central nervous system. In common usage, the term cerebrovascular disorders is not limited to conditions that affect the cerebrum, but refers to vascular disorders of the entire brain including the diencephalon; brain stem; and cerebellum. [NIH]

**Cerebrum:** The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

**Cervical:** Relating to the neck, or to the neck of any organ or structure. Cervical lymph nodes are located in the neck; cervical cancer refers to cancer of the uterine cervix, which is the lower, narrow end (the "neck") of the uterus. [NIH]

**Cervix:** The lower, narrow end of the uterus that forms a canal between the uterus and vagina. [NIH]

**Chamomile:** Common name for several daisy-like species native to Europe and Western Asia, now naturalized in the United States and Australia. The dried flower-heads of two species, Anthemis nobilis (Chamaemelum nobile) and Matricaria recutita, have specific use as herbs. They are administered as tea, extracts, tinctures, or ointments. Chamomile contains choline, coumarins, cyanogenic glycosides, flavonoids, salicylate derivatives, tannins, and volatile oils. [NIH]

**Character:** In current usage, approximately equivalent to personality. The sum of the relatively fixed personality traits and habitual modes of response of an individual. [NIH]

**Chemotactic Factors:** Chemical substances that attract or repel cells or organisms. The concept denotes especially those factors released as a result of tissue injury, invasion, or immunologic activity, that attract leukocytes, macrophages, or other cells to the site of infection or insult. [NIH]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Chest Pain: Pressure, burning, or numbress in the chest. [NIH]

**Chest wall:** The ribs and muscles, bones, and joints that make up the area of the body between the neck and the abdomen. [NIH]

**Chiropractic:** A system of treating bodily disorders by manipulation of the spine and other parts, based on the belief that the cause is the abnormal functioning of a nerve. [NIH]

**Chlorine:** A greenish-yellow, diatomic gas that is a member of the halogen family of elements. It has the atomic symbol Cl, atomic number 17, and atomic weight 70.906. It is a powerful irritant that can cause fatal pulmonary edema. Chlorine is used in manufacturing, as a reagent in synthetic chemistry, for water purification, and in the production of chlorinated lime, which is used in fabric bleaching. [NIH]

**Chloroform:** A commonly used laboratory solvent. It was previously used as an anesthetic, but was banned from use in the U.S. due to its suspected carcinogenecity. [NIH]

**Chlorophyll:** Porphyrin derivatives containing magnesium that act to convert light energy in photosynthetic organisms. [NIH]

**Chlorpromazine:** The prototypical phenothiazine antipsychotic drug. Like the other drugs in this class chlorpromazine's antipsychotic actions are thought to be due to long-term adaptation by the brain to blocking dopamine receptors. Chlorpromazine has several other actions and therapeutic uses, including as an antiemetic and in the treatment of intractable hiccup. [NIH]

**Cholera:** An acute diarrheal disease endemic in India and Southeast Asia whose causative agent is vibrio cholerae. This condition can lead to severe dehydration in a matter of hours unless quickly treated. [NIH]

**Cholera Toxin:** The enterotoxin from Vibrio cholerae. It is a protein that consists of two major components, the heavy (H) or A peptide and the light (L) or B peptide or choleragenoid. The B peptide anchors the protein to intestinal epithelial cells, while the A peptide, enters the cytoplasm, and activates adenylate cyclase, and production of cAMP. Increased levels of cAMP are thought to modulate release of fluid and electrolytes from intestinal crypt cells. [NIH]

**Cholesterol:** The principal sterol of all higher animals, distributed in body tissues, especially the brain and spinal cord, and in animal fats and oils. [NIH]

**Choline:** A basic constituent of lecithin that is found in many plants and animal organs. It is important as a precursor of acetylcholine, as a methyl donor in various metabolic processes, and in lipid metabolism. [NIH]

**Cholinergic:** Resembling acetylcholine in pharmacological action; stimulated by or releasing acetylcholine or a related compound. [EU]

**Chorea:** Involuntary, forcible, rapid, jerky movements that may be subtle or become confluent, markedly altering normal patterns of movement. Hypotonia and pendular reflexes are often associated. Conditions which feature recurrent or persistent episodes of chorea as a primary manifestation of disease are referred to as choreatic disorders. Chorea is also a frequent manifestation of basal ganglia diseases. [NIH]

**Choreatic Disorders:** Acquired and hereditary conditions which feature chorea as a primary manifestation of the disease process. [NIH]

**Chorioretinitis:** Inflammation of the choroid in which the sensory retina becomes edematous and opaque. The inflammatory cells and exudate may burst through the sensory retina to cloud the vitreous body. [NIH]

**Choroid:** The thin, highly vascular membrane covering most of the posterior of the eye between the retina and sclera. [NIH]

Chromosomal: Pertaining to chromosomes. [EU]

**Chromosome:** Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

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

Chronic Disease: Disease or ailment of long duration. [NIH]

**Chronic Fatigue Syndrome:** Fatigue caused by the combined effects of different types of prolonged fatigue. [NIH]

**Chronic renal:** Slow and progressive loss of kidney function over several years, often resulting in end-stage renal disease. People with end-stage renal disease need dialysis or transplantation to replace the work of the kidneys. [NIH]

**Circulatory system:** The system that contains the heart and the blood vessels and moves blood throughout the body. This system helps tissues get enough oxygen and nutrients, and it helps them get rid of waste products. The lymph system, which connects with the blood

system, is often considered part of the circulatory system. [NIH]

Citrus: Any tree or shrub of the Rue family or the fruit of these plants. [NIH]

Civilization: The distinctly human attributes and attainments of a particular society. [NIH]

**Clamp:** A u-shaped steel rod used with a pin or wire for skeletal traction in the treatment of certain fractures. [NIH]

**Classic Migraine:** Migraine preceded or accompanied by characteristic visual sensory disturbances, especially peripheral scintillations and hemianopsia. [NIH]

**Climacteric:** Physiologic period, characterized by endocrine, somatic, and psychic changes with the termination of ovarian function in the female. It may also accompany the normal diminution of sexual activity in the male. [NIH]

Clindamycin: An antibacterial agent that is a semisynthetic analog of lincomycin. [NIH]

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

**Clinical study:** A research study in which patients receive treatment in a clinic or other medical facility. Reports of clinical studies can contain results for single patients (case reports) or many patients (case series or clinical trials). [NIH]

**Clinical trial:** A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

**Clitoral:** Pertaining to the clitoris. [EU]

Clonic: Pertaining to or of the nature of clonus. [EU]

**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]

**Coagulation:** 1. The process of clot formation. 2. In colloid chemistry, the solidification of a sol into a gelatinous mass; an alteration of a disperse phase or of a dissolved solid which causes the separation of the system into a liquid phase and an insoluble mass called the clot or curd. Coagulation is usually irreversible. 3. In surgery, the disruption of tissue by physical means to form an amorphous residuum, as in electrocoagulation and photocoagulation. [EU]

**Coca:** Any of several South American shrubs of the Erythroxylon genus (and family) that yield cocaine; the leaves are chewed with alum for CNS stimulation. [NIH]

**Cocaine:** An alkaloid ester extracted from the leaves of plants including coca. It is a local anesthetic and vasoconstrictor and is clinically used for that purpose, particularly in the eye, ear, nose, and throat. It also has powerful central nervous system effects similar to the amphetamines and is a drug of abuse. Cocaine, like amphetamines, acts by multiple mechanisms on brain catecholaminergic neurons; the mechanism of its reinforcing effects is thought to involve inhibition of dopamine uptake. [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]

**Codeine:** An opioid analgesic related to morphine but with less potent analgesic properties and mild sedative effects. It also acts centrally to suppress cough. [NIH]

**Coenzyme:** An organic nonprotein molecule, frequently a phosphorylated derivative of a water-soluble vitamin, that binds with the protein molecule (apoenzyme) to form the active enzyme (holoenzyme). [EU]

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

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

**Cognitive restructuring:** A method of identifying and replacing fear-promoting, irrational beliefs with more realistic and functional ones. [NIH]

**Colic:** Paroxysms of pain. This condition usually occurs in the abdominal region but may occur in other body regions as well. [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]

**Collagen disease:** A term previously used to describe chronic diseases of the connective tissue (e.g., rheumatoid arthritis, systemic lupus erythematosus, and systemic sclerosis), but now is thought to be more appropriate for diseases associated with defects in collagen, which is a component of the connective tissue. [NIH]

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

**Colostrum:** The thin, yellow, serous fluid secreted by the mammary glands during pregnancy and immediately postpartum before lactation begins. It consists of immunologically active substances, white blood cells, water, protein, fat, and carbohydrates. [NIH]

**Comorbidity:** The presence of co-existing or additional diseases with reference to an initial diagnosis or with reference to the index condition that is the subject of study. Comorbidity may affect the ability of affected individuals to function and also their survival; it may be used as a prognostic indicator for length of hospital stay, cost factors, and outcome or survival. [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]

**Complement Activation:** The sequential activation of serum components C1 through C9, initiated by an erythrocyte-antibody complex or by microbial polysaccharides and properdin, and producing an inflammatory response. [NIH]

**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]

**Complete remission:** The disappearance of all signs of cancer. Also called a complete response. [NIH]

**Compress:** A plug used to occludate an orifice in the control of bleeding, or to mop up secretions; an absorbent pad. [NIH]

**Compulsive Behavior:** The behavior of performing an act persistently and repetitively without it leading to reward or pleasure. The act is usually a small, circumscribed behavior, almost ritualistic, yet not pathologically disturbing. Examples of compulsive behavior include twirling of hair, checking something constantly, not wanting pennies in change, straightening tilted pictures, etc. [NIH]

**Computational Biology:** A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

**Computed tomography:** CT scan. A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized tomography and computerized axial tomography (CAT) scan. [NIH]

**Computer Systems:** Systems composed of a computer or computers, peripheral equipment, such as disks, printers, and terminals, and telecommunications capabilities. [NIH]

**Computerized axial tomography:** A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called CAT scan, computed tomography (CT scan), or computerized tomography. [NIH]

**Computerized tomography:** A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized axial tomography (CAT) scan and computed tomography (CT scan). [NIH]

Concomitant: Accompanying; accessory; joined with another. [EU]

**Concretion:** Minute, hard, yellow masses found in the palpebral conjunctivae of elderly people or following chronic conjunctivitis, composed of the products of cellular degeneration retained in the depressions and tubular recesses in the conjunctiva. [NIH]

**Confusion:** A mental state characterized by bewilderment, emotional disturbance, lack of clear thinking, and perceptual disorientation. [NIH]

Congestion: Excessive or abnormal accumulation of blood in a part. [EU]

**Conjunctiva:** The mucous membrane that lines the inner surface of the eyelids and the anterior part of the sclera. [NIH]

**Conjunctivitis:** Inflammation of the conjunctiva, generally consisting of conjunctival hyperaemia associated with a discharge. [EU]

**Connective Tissue:** Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

**Connective Tissue:** Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

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

**Connexins:** A group of homologous proteins which form the intermembrane channels of gap junctions. The connexins are the products of an identified gene family which has both highly conserved and highly divergent regions. The variety contributes to the wide range of functional properties of gap junctions. [NIH]

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

Constipation: Infrequent or difficult evacuation of feces. [NIH]

**Constitutional:** 1. Affecting the whole constitution of the body; not local. 2. Pertaining to the constitution. [EU]

Constriction: The act of constricting. [NIH]

**Constriction, Pathologic:** The condition of an anatomical structure's being constricted beyond normal dimensions. [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]

**Continuum:** An area over which the vegetation or animal population is of constantly changing composition so that homogeneous, separate communities cannot be distinguished. [NIH]

**Contracture:** A condition of fixed high resistance to passive stretch of a muscle, resulting from fibrosis of the tissues supporting the muscles or the joints, or from disorders of the muscle fibres. [EU]

**Contraindications:** Any factor or sign that it is unwise to pursue a certain kind of action or treatment, e. g. giving a general anesthetic to a person with pneumonia. [NIH]

**Control group:** In a clinical trial, the group that does not receive the new treatment being studied. This group is compared to the group that receives the new treatment, to see if the new treatment works. [NIH]

**Controlled clinical trial:** A clinical study that includes a comparison (control) group. The comparison group receives a placebo, another treatment, or no treatment at all. [NIH]

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

[NIH]

**Convulsions:** A general term referring to sudden and often violent motor activity of cerebral or brainstem origin. Convulsions may also occur in the absence of an electrical cerebral discharge (e.g., in response to hypotension). [NIH]

**Convulsive:** Relating or referring to spasm; affected with spasm; characterized by a spasm or spasms. [NIH]

**Coordination:** Muscular or motor regulation or the harmonious cooperation of muscles or groups of muscles, in a complex action or series of actions. [NIH]

**Cor:** The muscular organ that maintains the circulation of the blood. c. adiposum a heart that has undergone fatty degeneration or that has an accumulation of fat around it; called also fat or fatty, heart. c. arteriosum the left side of the heart, so called because it contains oxygenated (arterial) blood. c. biloculare a congenital anomaly characterized by failure of formation of the atrial and ventricular septums, the heart having only two chambers, a single atrium and a single ventricle, and a common atrioventricular valve. c. bovinum (L. 'ox heart') a greatly enlarged heart due to a hypertrophied left ventricle; called also c. taurinum and bucardia. c. dextrum (L. 'right heart') the right atrium and ventricle. c. hirsutum, c. villosum. c. mobile (obs.) an abnormally movable heart. c. pendulum a heart so movable that it seems to be hanging by the great blood vessels. c. pseudotriloculare biatriatum a congenital cardiac anomaly in which the heart functions as a three-chambered heart because of tricuspid atresia, the right ventricle being extremely small or rudimentary and the right atrium greatly dilated. Blood passes from the right to the left atrium and thence disease due to pulmonary hypertension secondary to disease of the lung, or its blood vessels, with hypertrophy of the right ventricle. [EU]

**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 heart disease:** A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

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

**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]

**Corpus Luteum:** The yellow glandular mass formed in the ovary by an ovarian follicle that has ruptured and discharged its ovum. [NIH]

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

Cortical: Pertaining to or of the nature of a cortex or bark. [EU]

**Corticosteroids:** Hormones that have antitumor activity in lymphomas and lymphoid leukemias; in addition, corticosteroids (steroids) may be used for hormone replacement and for the management of some of the complications of cancer and its treatment. [NIH]

**Corticotropin-Releasing Hormone:** A neuropeptide released by the hypothalamus that stimulates the release of corticotropin by the anterior pituitary gland. [NIH]

**Cortisol:** A steroid hormone secreted by the adrenal cortex as part of the body's response to stress. [NIH]

**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]

**Coumarins:** Synthetic or naturally occurring substances related to coumarin, the deltalactone of coumarinic acid. Coumarin itself occurs in the tonka bean. The various coumarins have a wide range of proposed actions and uses including as anticoagulants, pharmaceutical aids, indicators and reagents, photoreactive substances, and antineoplastic agents. [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]

Craniotomy: An operation in which an opening is made in the skull. [NIH]

**Credentialing:** The recognition of professional or technical competence through registration, certification, licensure, admission to association membership, the award of a diploma or degree, etc. [NIH]

Criterion: A standard by which something may be judged. [EU]

Cryptococcosis: Infection with a fungus of the species Cryptococcus neoformans. [NIH]

**Cryptococcus:** A mitosporic Tremellales fungal genus whose species usually have a capsule and do not form pseudomycellium. Teleomorphs include Filobasidiella and Fidobasidium. [NIH]

**Cryptococcus neoformans:** A species of the fungus Cryptococcus, which causes cryptococcosis. Its teleomorph is Filobasidiella neoformans. [NIH]

**Cryptosporidiosis:** Parasitic intestinal infection with severe diarrhea caused by a protozoan, Cryptosporidium. It occurs in both animals and humans. [NIH]

**Cryptosporidium:** A genus of coccidian parasites of the family Cryptosporidiidae, found in the intestinal epithelium of many vertebrates including humans. [NIH]

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

Cutaneous: Having to do with the skin. [NIH]

**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]

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

Cysteine: A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

**Cystine:** A covalently linked dimeric nonessential amino acid formed by the oxidation of cysteine. Two molecules of cysteine are joined together by a disulfide bridge to form cystine. [NIH]

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

**Cytomegalovirus:** A genus of the family Herpesviridae, subfamily Betaherpesvirinae, infecting the salivary glands, liver, spleen, lungs, eyes, and other organs, in which they produce characteristically enlarged cells with intranuclear inclusions. Infection with

Cytomegalovirus is also seen as an opportunistic infection in AIDS. [NIH]

**Cytomegalovirus Infections:** Infection with Cytomegalovirus, characterized by enlarged cells bearing intranuclear inclusions. Infection may be in almost any organ, but the salivary glands are the most common site in children, as are the lungs in adults. [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]

Cytosine: A pyrimidine base that is a fundamental unit of nucleic acids. [NIH]

Cytotoxic: Cell-killing. [NIH]

Cytotoxic chemotherapy: Anticancer drugs that kill cells, especially cancer cells. [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]

**Decarboxylation:** The removal of a carboxyl group, usually in the form of carbon dioxide, from a chemical compound. [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]

**Decompression:** Decompression external to the body, most often the slow lessening of external pressure on the whole body (especially in caisson workers, deep sea divers, and persons who ascend to great heights) to prevent decompression sickness. It includes also sudden accidental decompression, but not surgical (local) decompression or decompression applied through body openings. [NIH]

**Decongestant:** An agent that reduces congestion or swelling. [EU]

**Degenerative:** Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Dehydration: The condition that results from excessive loss of body water. [NIH]

**Delivery of Health Care:** The concept concerned with all aspects of providing and distributing health services to a patient population. [NIH]

**Delusions:** A false belief regarding the self or persons or objects outside the self that persists despite the facts, and is not considered tenable by one's associates. [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]

**Dendrites:** Extensions of the nerve cell body. They are short and branched and receive stimuli from other neurons. [NIH]

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

**Dental Caries:** Localized destruction of the tooth surface initiated by decalcification of the enamel followed by enzymatic lysis of organic structures and leading to cavity formation. If left unchecked, the cavity may penetrate the enamel and dentin and reach the pulp. The three most prominent theories used to explain the etiology of the disase are that acids produced by bacteria lead to decalcification; that micro-organisms destroy the enamel protein; or that keratolytic micro-organisms produce chelates that lead to decalcification. [NIH]

**Dental Staff:** Personnel who provide dental service to patients in an organized facility, institution or agency. [NIH]

Dentists: Individuals licensed to practice dentistry. [NIH]

**Depersonalization:** Alteration in the perception of the self so that the usual sense of one's own reality is lost, manifested in a sense of unreality or self-estrangement, in changes of body image, or in a feeling that one does not control his own actions and speech; seen in depersonalization disorder, schizophrenic disorders, and schizotypal personality disorder. Some do not draw a distinction between depersonalization and derealization, using depersonalization to include both. [EU]

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]

**Depressive Disorder:** An affective disorder manifested by either a dysphoric mood or loss of interest or pleasure in usual activities. The mood disturbance is prominent and relatively persistent. [NIH]

**Derealization:** Is characterized by the loss of the sense of reality concerning one's surroundings. [NIH]

Dermatitis: Any inflammation of the skin. [NIH]

**Dermatitis Herpetiformis:** Rare, chronic, papulo-vesicular disease characterized by an intensely pruritic eruption consisting of various combinations of symmetrical, erythematous, papular, vesicular, or bullous lesions. The disease is strongly associated with the presence of HLA-B8 and HLA-DR3 antigens. A variety of different autoantibodies has been detected in small numbers in patients with dermatitis herpetiformis. [NIH]

Dermatosis: Any skin disease, especially one not characterized by inflammation. [EU]

**Deuterium:** Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [NIH]

**Developed Countries:** Countries that have reached a level of economic achievement through an increase of production, per capita income and consumption, and utilization of natural and human resources. [NIH]

**Dexamethasone:** (11 beta,16 alpha)-9-Fluoro-11,17,21-trihydroxy-16-methylpregna-1,4diene-3,20-dione. An anti-inflammatory glucocorticoid used either in the free alcohol or esterified form in treatment of conditions that respond generally to cortisone. [NIH]

**Dextromethorphan:** The d-isomer of the codeine analog of levorphanol. Dextromethorphan shows high affinity binding to several regions of the brain, including the medullary cough center. This compound is a NMDA receptor antagonist (receptors, N-methyl-D-aspartate) and acts as a non-competitive channel blocker. It is used widely as an antitussive agent, and is also used to study the involvement of glutamate receptors in neurotoxicity. [NIH]

**DHEA:** Dehydroepiandrosterone. A substance that is being studied as a cancer prevention drug. It belongs to the family of drugs called steroids. [NIH]

**Diabetes Mellitus:** A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

**Diabetic Retinopathy:** Retinopathy associated with diabetes mellitus, which may be of the background type, progressively characterized by microaneurysms, interretinal punctuate macular edema, or of the proliferative type, characterized by neovascularization of the retina and optic disk, which may project into the vitreous, proliferation of fibrous tissue, vitreous hemorrhage, and retinal detachment. [NIH]

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

**Dialyzer:** A part of the hemodialysis machine. (See hemodialysis under dialysis.) The dialyzer has two sections separated by a membrane. One section holds dialysate. The other holds the patient's blood. [NIH]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diarrhoea: Abnormal frequency and liquidity of faecal discharges. [EU]

Diastolic: Of or pertaining to the diastole. [EU]

**Diastolic blood pressure:** The minimum pressure that remains within the artery when the heart is at rest. [NIH]

**Diclofenac:** A non-steroidal anti-inflammatory agent (NSAID) with antipyretic and analgesic actions. It is primarily available as the sodium salt, diclofenac sodium. [NIH]

**Diclofenac Sodium:** The sodium form of diclofenac. It is used for its analgesic and antiinflammatory properties. [NIH]

**Diencephalon:** The paired caudal parts of the prosencephalon from which the thalamus, hypothalamus, epithalamus, and subthalamus are derived. [NIH]

**Diffusion:** The tendency of a gas or solute to pass from a point of higher pressure or concentration to a point of lower pressure or concentration and to distribute itself throughout the available space; a major mechanism of biological transport. [NIH]

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

**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]

**Dihydroergotamine:** A derivative of ergotamine prepared by the catalytic hydrogenation of ergotamine. It is used as a vasoconstrictor, specifically for the therapy of migraine. [NIH]

**Dilatation:** The act of dilating. [NIH]

**Dilatation, Pathologic:** The condition of an anatomical structure's being dilated beyond normal dimensions. [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]

Dilator: A device used to stretch or enlarge an opening. [NIH]

Diploid: Having two sets of chromosomes. [NIH]

**Diplopia:** A visual symptom in which a single object is perceived by the visual cortex as two objects rather than one. Disorders associated with this condition include refractive errors; strabismus; oculomotor nerve diseases; trochlear nerve diseases; abducens nerve diseases; and diseases of the brain stem and occipital lobe. [NIH]

**Direct:** 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

**Discrimination:** The act of qualitative and/or quantitative differentiation between two or more stimuli. [NIH]

**Disease Progression:** The worsening of a disease over time. This concept is most often used for chronic and incurable diseases where the stage of the disease is an important determinant of therapy and prognosis. [NIH]

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

**Diskectomy:** Excision, in part or whole, of an intervertebral disk. The most common indication is disk displacement or herniation. In addition to standard surgical removal, it can be performed by percutaneous diskectomy or by laparoscopic diskectomy, the former being the more common. [NIH]

**Disorientation:** The loss of proper bearings, or a state of mental confusion as to time, place, or identity. [EU]

**Disparity:** Failure of the two retinal images of an object to fall on corresponding retinal points. [NIH]

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

**Dissociation:** 1. The act of separating or state of being separated. 2. The separation of a molecule into two or more fragments (atoms, molecules, ions, or free radicals) produced by the absorption of light or thermal energy or by solvation. 3. In psychology, a defense mechanism in which a group of mental processes are segregated from the rest of a person's mental activity in order to avoid emotional distress, as in the dissociative disorders (q.v.), or in which an idea or object is segregated from its emotional significance; in the first sense it is roughly equivalent to splitting, in the second, to isolation. 4. A defect of mental integration in which one or more groups of mental processes become separated off from normal consciousness and, thus separated, function as a unitary whole. [EU]

**Distal:** Remote; farther from any point of reference; opposed to proximal. In dentistry, used to designate a position on the dental arch farther from the median line of the jaw. [EU]

**Diuresis:** Increased excretion of urine. [EU]

Diurnal: Occurring during the day. [EU]

**Diving:** An activity in which the organism plunges into water. It includes scuba and bell diving. Diving as natural behavior of animals goes here, as well as diving in decompression experiments with humans or animals. [NIH]

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

**Dominance:** In genetics, the full phenotypic expression of a gene in both heterozygotes and homozygotes. [EU]

**Dopamine:** An endogenous catecholamine and prominent neurotransmitter in several systems of the brain. In the synthesis of catecholamines from tyrosine, it is the immediate precursor to norepinephrine and epinephrine. Dopamine is a major transmitter in the extrapyramidal system of the brain, and important in regulating movement. A family of dopaminergic receptor subtypes mediate its action. Dopamine is used pharmacologically for its direct (beta adrenergic agonist) and indirect (adrenergic releasing) sympathomimetic effects including its actions as an inotropic agent and as a renal vasodilator. [NIH]

Dopamine Agonists: Drugs that bind to and activate dopamine receptors. [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]

Dorsum: A plate of bone which forms the posterior boundary of the sella turcica. [NIH]

**Dosage Forms:** Completed forms of the pharmaceutical preparation in which prescribed doses of medication are included. They are designed to resist action by gastric fluids, prevent vomiting and nausea, reduce or alleviate the undesirable taste and smells associated with oral administration, achieve a high concentration of drug at target site, or produce a delayed or long-acting drug effect. They include capsules, liniments, ointments, pharmaceutical solutions, powders, tablets, etc. [NIH]

**Double-blinded:** A clinical trial in which neither the medical staff nor the person knows which of several possible therapies the person is receiving. [NIH]

**Doxycycline:** A synthetic tetracycline derivative with a range of antimicrobial activity and mode of action similar to that of tetracycline, but more effective against many species. Animal studies suggest that it may cause less tooth staining than other tetracyclines. [NIH]

Drip: The continuous slow introduction of a fluid containing nutrients or drugs. [NIH]

**Drive:** A state of internal activity of an organism that is a necessary condition before a given stimulus will elicit a class of responses; e.g., a certain level of hunger (drive) must be present before food will elicit an eating response. [NIH]

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

**Drug Tolerance:** Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

**Dry Eye Syndrome:** A common condition that occurs when the eyes do not produce enough tears to keep the eye moist and comfortable. Common symptoms of dry eye include pain, stinging, burning, scratchiness, and intermittent blurring of vision. [NIH]

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

**Duodenal Ulcer:** An ulcer in the lining of the first part of the small intestine (duodenum). [NIH]

Duodenum: The first part of the small intestine. [NIH]

**Dura mater:** The outermost, toughest, and most fibrous of the three membranes (meninges) covering the brain and spinal cord; called also pachymeninx. [EU]

**Dyes:** Chemical substances that are used to stain and color other materials. The coloring may or may not be permanent. Dyes can also be used as therapeutic agents and test reagents in medicine and scientific research. [NIH]

**Dyskinesia:** Impairment of the power of voluntary movement, resulting in fragmentary or incomplete movements. [EU]

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

Dyspepsia: Impaired digestion, especially after eating. [NIH]

**Dysphagia:** Difficulty in swallowing. [EU]

Dysphonia: Difficulty or pain in speaking; impairment of the voice. [NIH]

**Dysphoria:** Disquiet; restlessness; malaise. [EU]

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

Dyspnea: Difficult or labored breathing. [NIH]

Dystonia: Disordered tonicity of muscle. [EU]

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

Earache: Pain in the ear. [NIH]

**Early Ambulation:** Procedure characterized by a shorter period of hospitalization or recumbency or by more rapid mobilization than is normally practiced. [NIH]

**Eating Disorders:** A group of disorders characterized by physiological and psychological disturbances in appetite or food intake. [NIH]

**Eczema:** A pruritic papulovesicular dermatitis occurring as a reaction to many endogenous and exogenous agents (Dorland, 27th ed). [NIH]

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

**Effector:** It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

**Effector cell:** A cell that performs a specific function in response to a stimulus; usually used to describe cells in the immune system. [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]

Elasticity: Resistance and recovery from distortion of shape. [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]

**Electroconvulsive Therapy:** Electrically induced convulsions primarily used in the treatment of severe affective disorders and schizophrenia. [NIH]

**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]

**Electrophoresis:** An electrochemical process in which macromolecules or colloidal particles with a net electric charge migrate in a solution under the influence of an electric current. [NIH]

**Electrophysiological:** Pertaining to electrophysiology, that is a branch of physiology that is concerned with the electric phenomena associated with living bodies and involved in their functional activity. [EU]

**Elementary Particles:** Individual components of atoms, usually subatomic; subnuclear particles are usually detected only when the atomic nucleus decays and then only transiently, as most of them are unstable, often yielding pure energy without substance, i.e., radiation. [NIH]

Emboli: Bit of foreign matter which enters the blood stream at one point and is carried until

it is lodged or impacted in an artery and obstructs it. It may be a blood clot, an air bubble, fat or other tissue, or clumps of bacteria. [NIH]

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

**Emesis:** Vomiting; an act of vomiting. Also used as a word termination, as in haematemesis. [EU]

Emetic: An agent that causes vomiting. [EU]

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

**Encephalitis:** Inflammation of the brain due to infection, autoimmune processes, toxins, and other conditions. Viral infections (see encephalitis, viral) are a relatively frequent cause of this condition. [NIH]

**Encephalitis, Viral:** Inflammation of brain parenchymal tissue as a result of viral infection. Encephalitis may occur as primary or secondary manifestation of Togaviridae infections; Herpesviridae infections; Adenoviridae infections; Flaviviridae infections; Bunyaviridae infections; Picornaviridae infections; Paramyxoviridae infections; Orthomyxoviridae infections; Retroviridae infections; and Arenaviridae infections. [NIH]

**Encephalopathy:** A disorder of the brain that can be caused by disease, injury, drugs, or chemicals. [NIH]

**Endemic:** Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

**Endocarditis:** Exudative and proliferative inflammatory alterations of the endocardium, characterized by the presence of vegetations on the surface of the endocardium or in the endocardium itself, and most commonly involving a heart valve, but sometimes affecting the inner lining of the cardiac chambers or the endocardium elsewhere. It may occur as a primary disorder or as a complication of or in association with another disease. [EU]

**Endocrine System:** The system of glands that release their secretions (hormones) directly into the circulatory system. In addition to the endocrine glands, included are the chromaffin system and the neurosecretory systems. [NIH]

Endometrium: The layer of tissue that lines the uterus. [NIH]

**Endothelial cell:** The main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart. [NIH]

**Endothelium:** A layer of epithelium that lines the heart, blood vessels (endothelium, vascular), lymph vessels (endothelium, lymphatic), and the serous cavities of the body. [NIH]

**Endothelium, Lymphatic:** Unbroken cellular lining (intima) of the lymph vessels (e.g., the high endothelial lymphatic venules). It is more permeable than vascular endothelium, lacking selective absorption and functioning mainly to remove plasma proteins that have filtered through the capillaries into the tissue spaces. [NIH]

**Endothelium, Vascular:** Single pavement layer of cells which line the luminal surface of the entire vascular system and regulate the transport of macromolecules and blood components from interstitium to lumen; this function has been most intensively studied in the blood capillaries. [NIH]

**Endothelium-derived:** Small molecule that diffuses to the adjacent muscle layer and relaxes it. [NIH]

**Endotoxic:** Of, relating to, or acting as an endotoxin (= a heat-stable toxin, associated with the outer membranes of certain gram-negative bacteria. Endotoxins are not secreted and are

released only when the cells are disrupted). [EU]

Endotoxin: Toxin from cell walls of bacteria. [NIH]

**End-stage renal:** Total chronic kidney failure. When the kidneys fail, the body retains fluid and harmful wastes build up. A person with ESRD needs treatment to replace the work of the failed kidneys. [NIH]

**Energy balance:** Energy is the capacity of a body or a physical system for doing work. Energy balance is the state in which the total energy intake equals total energy needs. [NIH]

**Enuresis:** Involuntary discharge of urine after the age at which urinary control should have been achieved; often used alone with specific reference to involuntary discharge of urine occurring during sleep at night (bed-wetting, nocturnal enuresis). [EU]

**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]

**Eosinophilic:** A condition found primarily in grinding workers caused by a reaction of the pulmonary tissue, in particular the eosinophilic cells, to dust that has entered the lung. [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]

**Ependyma:** A thin membrane that lines the ventricles of the brain and the central canal of the spinal cord. [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]

Epidemiological: Relating to, or involving epidemiology. [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]

**Epidural:** The space between the wall of the spinal canal and the covering of the spinal cord. An epidural injection is given into this space. [NIH]

Epidural Space: Space between the dura mater and the walls of the vertebral canal. [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]

**Ergot:** Cataract due to ergot poisoning caused by eating of rye cereals contaminated by a fungus. [NIH]

**Ergot Alkaloids:** Alkaloids isolated from the ergot fungus Claviceps purpurea (Hypocreaceae). The ergot alkaloids were the first alpha-adrenergic antagonists discovered, but side effects generally prevent their administration in doses that would produce more than a minimal blockade in humans. Their smooth muscle-stimulating activities may be attributed to alpha-agonistic properties, thus characterizing these alkaloids as a series of partial agonists. They have many clinical applications, notably in obstetrics and the treatment of migraine. (From Martindale, The Extra Pharmacopoeia, 28th ed, p662). [NIH]

**Ergotamine:** A vasoconstrictor found in ergot of Central Europe. It is an alpha-1 selective adrenergic agonist and is commonly used in the treatment of migraine headaches. [NIH]

**Ergotism:** Poisoning caused by ingesting ergotized grain or by the misdirected or excessive use of ergot as a medicine. [NIH]

**Erythema:** Redness of the skin produced by congestion of the capillaries. This condition may result from a variety of causes. [NIH]

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

**Erythromycin:** A bacteriostatic antibiotic substance produced by Streptomyces erythreus. Erythromycin A is considered its major active component. In sensitive organisms, it inhibits protein synthesis by binding to 50S ribosomal subunits. This binding process inhibits peptidyl transferase activity and interferes with translocation of amino acids during translation and assembly of proteins. [NIH]

**Escalation:** Progressive use of more harmful drugs. [NIH]

**Esophagus:** The muscular tube through which food passes from the throat to the stomach. [NIH]

**Esotropia:** A form of ocular misalignment characterized by an excessive convergence of the visual axes, resulting in a "cross-eye" appearance. An example of this condition occurs when paralysis of the lateral rectus muscle causes an abnormal inward deviation of one eye on attempted gaze. [NIH]

**Essential Tremor:** A rhythmic, involuntary, purposeless, oscillating movement resulting from the alternate contraction and relaxation of opposing groups of muscles. [NIH]

**Estrogen:** One of the two female sex hormones. [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]

**Ethmoid:** An unpaired cranial bone which helps form the medial walls of the orbits and contains the themoidal air cells which drain into the nose. [NIH]

**Eucalyptus:** A genus of Australian trees of the Myrtaceae family that yields gums, oils, and resins which are used as flavoring agents, astringents, and aromatics, and formerly to treat diarrhea, asthma, bronchitis, and respiratory tract infections. [NIH]

**Eukaryotic Cells:** Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

**Evacuation:** An emptying, as of the bowels. [EU]

**Evoke:** The electric response recorded from the cerebral cortex after stimulation of a peripheral sense organ. [NIH]

**Excipients:** Usually inert substances added to a prescription in order to provide suitable consistency to the dosage form; a binder, matrix, base or diluent in pills, tablets, creams, salves, etc. [NIH]

**Excitability:** Property of a cardiac cell whereby, when the cell is depolarized to a critical level (called threshold), the membrane becomes permeable and a regenerative inward current causes an action potential. [NIH]

**Excitation:** An act of irritation or stimulation or of responding to a stimulus; the addition of energy, as the excitation of a molecule by absorption of photons. [EU]

**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]

**Excitatory Amino Acids:** Endogenous amino acids released by neurons as excitatory neurotransmitters. Glutamic acid is the most common excitatory neurotransmitter in the brain. Aspartic acid has been regarded as an excitatory transmitter for many years, but the extent of its role as a transmitter is unclear. [NIH]

**Excitotoxicity:** Excessive exposure to glutamate or related compounds can kill brain neurons, presumably by overstimulating them. [NIH]

Excrete: To get rid of waste from the body. [NIH]

Exhaustion: The feeling of weariness of mind and body. [NIH]

**Exocytosis:** Cellular release of material within membrane-limited vesicles by fusion of the vesicles with the cell membrane. [NIH]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

**Exon:** The part of the DNA that encodes the information for the actual amino acid sequence of the protein. In many eucaryotic genes, the coding sequences consist of a series of exons alternating with intron sequences. [NIH]

**Exotropia:** A form of ocular misalignment where the visual axes diverge inappropriately. For example, medial rectus muscle weakness may produce this condition as the affected eye will deviate laterally upon attempted forward gaze. An exotropia occurs due to the relatively unopposed force exerted on the eye by the lateral rectus muscle, which pulls the eye in an outward direction. [NIH]

**Expectorant:** 1. Promoting the ejection, by spitting, of mucus or other fluids from the lungs and trachea. 2. An agent that promotes the ejection of mucus or exudate from the lungs, bronchi, and trachea; sometimes extended to all remedies that quiet cough (antitussives). [EU]

**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]

Extraction: The process or act of pulling or drawing out. [EU]

Extrapyramidal: Outside of the pyramidal tracts. [EU]

Extravasation: A discharge or escape, as of blood, from a vessel into the tissues. [EU]

**Extremity:** A limb; an arm or leg (membrum); sometimes applied specifically to a hand or foot. [EU]

**Exudate:** Material, such as fluid, cells, or cellular debris, which has escaped from blood vessels and has been deposited in tissues or on tissue surfaces, usually as a result of inflammation. An exudate, in contrast to a transudate, is characterized by a high content of protein, cells, or solid materials derived from cells. [EU]

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

**Facial Pain:** Pain in the facial region including orofacial pain and craniofacial pain. Associated conditions include local inflammatory and neoplastic disorders and neuralgic syndromes involving the trigeminal, facial, and glossopharyngeal nerves. Conditions which feature recurrent or persistent facial pain as the primary manifestation of disease are referred to as facial pain syndromes. [NIH]

**Family Planning:** Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Fascioliasis: Helminth infection of the liver caused by species of Fasciola. [NIH]

Fat: Total lipids including phospholipids. [NIH]

**Fatigue:** The state of weariness following a period of exertion, mental or physical, characterized by a decreased capacity for work and reduced efficiency to respond to stimuli. [NIH]

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

Febrile: Pertaining to or characterized by fever. [EU]

**Feces:** The excrement discharged from the intestines, consisting of bacteria, cells exfoliated from the intestines, secretions, chiefly of the liver, and a small amount of food residue. [EU]

**Feeding Behavior:** Behavioral responses or sequences associated with eating including modes of feeding, rhythmic patterns of eating, and time intervals. [NIH]

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

**Fibrin:** A protein derived from fibrinogen in the presence of thrombin, which forms part of the blood clot. [NIH]

**Fibrinogen:** Plasma glycoprotein clotted by thrombin, composed of a dimer of three nonidentical pairs of polypeptide chains (alpha, beta, gamma) held together by disulfide bonds. Fibrinogen clotting is a sol-gel change involving complex molecular arrangements: whereas fibrinogen is cleaved by thrombin to form polypeptides A and B, the proteolytic action of other enzymes yields different fibrinogen degradation products. [NIH]

**Fibrosis:** Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

**Fibrositis:** Aching, soreness or stiffness of muscles; often caused by inexpedient work postures. [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]

Fixation: 1. The act or operation of holding, suturing, or fastening in a fixed position. 2. The

condition of being held in a fixed position. 3. In psychiatry, a term with two related but distinct meanings : (1) arrest of development at a particular stage, which like regression (return to an earlier stage), if temporary is a normal reaction to setbacks and difficulties but if protracted or frequent is a cause of developmental failures and emotional problems, and (2) a close and suffocating attachment to another person, especially a childhood figure, such as one's mother or father. Both meanings are derived from psychoanalytic theory and refer to 'fixation' of libidinal energy either in a specific erogenous zone, hence fixation at the oral, anal, or phallic stage, or in a specific object, hence mother or father fixation. 4. The use of a fixative (q.v.) to preserve histological or cytological specimens. 5. In chemistry, the process whereby a substance is removed from the gaseous or solution phase and localized, as in carbon dioxide fixation or nitrogen fixation. 6. In ophthalmology, direction of the gaze so that the visual image of the object falls on the fovea centralis. 7. In film processing, the chemical removal of all undeveloped salts of the film emulsion, leaving only the developed silver to form a permanent image. [EU]

Flatus: Gas passed through the rectum. [NIH]

**Flavoring Agents:** Substances added to foods and medicine to improve the quality of taste. [NIH]

**Fluconazole:** Triazole antifungal agent that is used to treat oropharyngeal candidiasis and cryptococcal meningitis in AIDS. [NIH]

Flucytosine: A fluorinated cytosine analog that is used as an antifungal agent. [NIH]

**Flunarizine:** Flunarizine is a selective calcium entry blocker with calmodulin binding properties and histamine H1 blocking activity. It is effective in the prophylaxis of migraine, occlusive peripheral vascular disease, vertigo of central and peripheral origin, and as an adjuvant in the therapy of epilepsy. [NIH]

**Fluorine:** A nonmetallic, diatomic gas that is a trace element and member of the halogen family. It is used in dentistry as flouride to prevent dental caries. [NIH]

**Flushing:** A transient reddening of the face that may be due to fever, certain drugs, exertion, stress, or a disease process. [NIH]

Fold: A plication or doubling of various parts of the body. [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]

**Fourth Ventricle:** An irregularly shaped cavity in the rhombencephalon, between the medulla oblongata, the pons, and the isthmus in front, and the cerebellum behind. It is continuous with the central canal of the cord below and with the cerebral aqueduct above, and through its lateral and median apertures it communicates with the subarachnoid space. [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]

Frontal Lobe: The anterior part of the cerebral hemisphere. [NIH]

**Fungi:** A kingdom of eukaryotic, heterotrophic organisms that live as saprobes or parasites, including mushrooms, yeasts, smuts, molds, etc. They reproduce either sexually or asexually, and have life cycles that range from simple to complex. Filamentous fungi refer to those that grow as multicelluar colonies (mushrooms and molds). [NIH]

**Fungus:** A general term used to denote a group of eukaryotic protists, including mushrooms, yeasts, rusts, moulds, smuts, etc., which are characterized by the absence of chlorophyll and by the presence of a rigid cell wall composed of chitin, mannans, and

sometimes cellulose. They are usually of simple morphological form or show some reversible cellular specialization, such as the formation of pseudoparenchymatous tissue in the fruiting body of a mushroom. The dimorphic fungi grow, according to environmental conditions, as moulds or yeasts. [EU]

**Gallbladder:** The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

**Gamma Rays:** Very powerful and penetrating, high-energy electromagnetic radiation of shorter wavelength than that of x-rays. They are emitted by a decaying nucleus, usually between 0.01 and 10 MeV. They are also called nuclear x-rays. [NIH]

**Ganciclovir:** Acyclovir analog that is a potent inhibitor of the Herpesvirus family including cytomegalovirus. Ganciclovir is used to treat complications from AIDS-associated cytomegalovirus infections. [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]

**Gap Junctions:** Connections between cells which allow passage of small molecules and electric current. Gap junctions were first described anatomically as regions of close apposition between cells with a narrow (1-2 nm) gap between cell membranes. The variety in the properties of gap junctions is reflected in the number of connexins, the family of proteins which form the junctions. [NIH]

**Gas:** Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastric Acid: Hydrochloric acid present in gastric juice. [NIH]

**Gastric Juices:** Liquids produced in the stomach to help break down food and kill bacteria. [NIH]

**Gastrin:** A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

**Gastroenteritis:** An acute inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhoea, abdominal pain, and weakness, which has various causes, including food poisoning due to infection with such organisms as Escherichia coli, Staphylococcus aureus, and Salmonella species; consumption of irritating food or drink; or psychological factors such as anger, stress, and fear. Called also enterogastritis. [EU]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [NIH]

**Gelatin:** A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [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 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 Techniques:** Chromosomal, biochemical, intracellular, and other methods used in the study of genetics. [NIH]

**Genetics:** The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genital: Pertaining to the genitalia. [EU]

Genitourinary: Pertaining to the genital and urinary organs; urogenital; urinosexual. [EU]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Germ Cells: The reproductive cells in multicellular organisms. [NIH]

**Gestation:** The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

**Ginseng:** An araliaceous genus of plants that contains a number of pharmacologically active agents used as stimulants, sedatives, and tonics, especially in traditional medicine. [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]

**Glossopharyngeal Nerve:** The 9th cranial nerve. The glossopharyngeal nerve is a mixed motor and sensory nerve; it conveys somatic and autonomic efferents as well as general, special, and visceral afferents. Among the connections are motor fibers to the stylopharyngeus muscle, parasympathetic fibers to the parotid glands, general and taste afferents from the posterior third of the tongue, the nasopharynx, and the palate, and afferents from baroreceptors and chemoreceptors of the carotid sinus. [NIH]

**Glucocorticoid:** A compound that belongs to the family of compounds called corticosteroids (steroids). Glucocorticoids affect metabolism and have anti-inflammatory and immunosuppressive effects. They may be naturally produced (hormones) or synthetic (drugs). [NIH]

**Glucose:** D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

**Glucose Intolerance:** A pathological state in which the fasting plasma glucose level is less than 140 mg per deciliter and the 30-, 60-, or 90-minute plasma glucose concentration following a glucose tolerance test exceeds 200 mg per deciliter. This condition is seen frequently in diabetes mellitus but also occurs with other diseases. [NIH]

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]

**Glycine:** A non-essential amino acid. It is found primarily in gelatin and silk fibroin and used therapeutically as a nutrient. It is also a fast inhibitory neurotransmitter. [NIH]

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]

**Gonad:** A sex organ, such as an ovary or a testicle, which produces the gametes in most multicellular animals. [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]

**Grade:** The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

**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]

**Gram-positive:** Retaining the stain or resisting decolorization by alcohol in Gram's method of staining, a primary characteristic of bacteria whose cell wall is composed of a thick layer of peptidologlycan with attached teichoic acids. [EU]

**Granulocytes:** Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

**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]

**Guanylate Cyclase:** An enzyme that catalyzes the conversion of GTP to 3',5'-cyclic GMP and pyrophosphate. It also acts on ITP and dGTP. (From Enzyme Nomenclature, 1992) EC 4.6.1.2. [NIH]

Haematemesis: The vomiting of blood. [EU]

Hair follicles: Shafts or openings on the surface of the skin through which hair grows. [NIH]

**Half-Life:** The time it takes for a substance (drug, radioactive nuclide, or other) to lose half of its pharmacologic, physiologic, or radiologic activity. [NIH]

**Haploid:** An organism with one basic chromosome set, symbolized by n; the normal condition of gametes in diploids. [NIH]

**Haptens:** Small antigenic determinants capable of eliciting an immune response only when coupled to a carrier. Haptens bind to antibodies but by themselves cannot elicit an antibody response. [NIH]

**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]

**Headache Disorders:** Common conditions characterized by persistent or recurrent headaches. Headache syndrome classification systems may be based on etiology (e.g., vascular headache, post-traumatic headaches, etc.), temporal pattern (e.g., cluster headache, paroxysmal hemicrania, etc.), and precipitating factors (e.g., cough headache). [NIH]

**Health Care Costs:** The actual costs of providing services related to the delivery of health care, including the costs of procedures, therapies, and medications. It is differentiated from health expenditures, which refers to the amount of money paid for the services, and from fees, which refers to the amount charged, regardless of cost. [NIH]

**Health Expenditures:** The amounts spent by individuals, groups, nations, or private or public organizations for total health care and/or its various components. These amounts may or may not be equivalent to the actual costs (health care costs) and may or may not be shared among the patient, insurers, and/or employers. [NIH]

**Health Promotion:** Encouraging consumer behaviors most likely to optimize health potentials (physical and psychosocial) through health information, preventive programs, and access to medical care. [NIH]

**Health Services:** Services for the diagnosis and treatment of disease and the maintenance of health. [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]

Heart attack: A seizure of weak or abnormal functioning of the heart. [NIH]

**Heartburn:** Substernal pain or burning sensation, usually associated with regurgitation of gastric juice into the esophagus. [NIH]

Hematoma: An extravasation of blood localized in an organ, space, or tissue. [NIH]

**Hemianopsia:** Partial or complete loss of vision in one half of the visual field(s) of one or both eyes. Subtypes include altitudinal hemianopsia, characterized by a visual defect above or below the horizontal meridian of the visual field. Homonymous hemianopsia refers to a visual defect that affects both eyes equally, and occurs either to the left or right of the midline of the visual field. Binasal hemianopsia consists of loss of vision in the nasal hemifields of both eyes. Bitemporal hemianopsia is the bilateral loss of vision in the temporal fields. Quadrantanopsia refers to loss of vision in one quarter of the visual field in one or both eyes. [NIH]

Hemicrania: An ache or a pain in one side of the head, as in migraine. [NIH]

Hemiparesis: The weakness or paralysis affecting one side of the body. [NIH]

**Hemiplegia:** Severe or complete loss of motor function on one side of the body. This condition is usually caused by BRAIN DISEASES that are localized to the cerebral hemisphere opposite to the side of weakness. Less frequently, BRAIN STEM lesions; cervical spinal cord diseases; peripheral nervous system diseases; and other conditions may manifest as hemiplegia. The term hemiparesis (see paresis) refers to mild to moderate weakness involving one side of the body. [NIH]

**Hemodialysis:** The use of a machine to clean wastes from the blood after the kidneys have failed. The blood travels through tubes to a dialyzer, which removes wastes and extra fluid. The cleaned blood then flows through another set of tubes back into the body. [NIH]

**Hemodynamics:** The movements of the blood and the forces involved in systemic or regional blood circulation. [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]

**Hemoglobin A:** Normal adult human hemoglobin. The globin moiety consists of two alpha and two beta chains. [NIH]

Hemoglobinuria: The presence of free hemoglobin in the urine. [NIH]

**Hemolysis:** The destruction of erythrocytes by many different causal agents such as antibodies, bacteria, chemicals, temperature, and changes in tonicity. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

**Hemorrhagic stroke:** A disorder involving bleeding within ischemic brain tissue. Hemorrhagic stroke occurs when blood vessels that are damaged or dead from lack of blood supply (infarcted), located within an area of infarcted brain tissue, rupture and transform an "ischemic" stroke into a hemorrhagic stroke. Ischemia is inadequate tissue oxygenation caused by reduced blood flow; infarction is tissue death resulting from ischemia. Bleeding irritates the brain tissues, causing swelling (cerebral edema). Blood collects into a mass (hematoma). Both swelling and hematoma will compress and displace brain tissue. [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]

**Herpes:** Any inflammatory skin disease caused by a herpesvirus and characterized by the formation of clusters of small vesicles. When used alone, the term may refer to herpes simplex or to herpes zoster. [EU]

Herpes Zoster: Acute vesicular inflammation. [NIH]

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]

**Heterotropia:** One in which the angle of squint remains relatively unaltered on conjugate movement of the eyes. [NIH]

**Hiccup:** A spasm of the diaphragm that causes a sudden inhalation followed by rapid closure of the glottis which produces a sound. [NIH]

**Histamine:** 1H-Imidazole-4-ethanamine. A depressor amine derived by enzymatic decarboxylation of histidine. It is a powerful stimulant of gastric secretion, a constrictor of bronchial smooth muscle, a vasodilator, and also a centrally acting neurotransmitter. [NIH]

**Histidine:** An essential amino acid important in a number of metabolic processes. It is required for the production of histamine. [NIH]

Histology: The study of tissues and cells under a microscope. [NIH]

**Homeostasis:** The processes whereby the internal environment of an organism tends to remain balanced and stable. [NIH]

**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]

Homotypic: Adhesion between neutrophils. [NIH]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

**Hormone:** A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

**Hormone Replacement Therapy:** Therapeutic use of hormones to alleviate the effects of hormone deficiency. [NIH]

**Hormone therapy:** Treatment of cancer by removing, blocking, or adding hormones. Also called endocrine therapy. [NIH]

Host: Any animal that receives a transplanted graft. [NIH]

**Humeral:** 1. Of, relating to, or situated in the region of the humerus: brachial. 2. Of or belonging to the shoulder. 3. Of, relating to, or being any of several body parts that are analogous in structure, function, or location to the humerus or shoulder. [EU]

**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]

**Hydrophilic:** Readily absorbing moisture; hygroscopic; having strongly polar groups that readily interact with water. [EU]

**Hydrophobic:** Not readily absorbing water, or being adversely affected by water, as a hydrophobic colloid. [EU]

**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]

Hyperalgesia: Excessive sensitiveness or sensibility to pain. [EU]

**Hyperesthesia:** Increased sensitivity to cutaneous stimulation due to a diminished threshold or an increased response to stimuli. [NIH]

Hyperglycemia: Abnormally high blood sugar. [NIH]

Hyperkinesia: Abnormally increased motor function or activity; hyperactivity. [EU]

Hypersecretion: Excessive secretion. [EU]

**Hypersensitivity:** Altered reactivity to an antigen, which can result in pathologic reactions upon subsequent exposure to that particular antigen. [NIH]

**Hypertension:** Persistently high arterial blood pressure. Currently accepted threshold levels are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [NIH]

**Hypertensive Encephalopathy:** Brain dysfunction or damage resulting from malignant hypertension, usually associated with a diastolic blood pressure in excess of 125 mmHg. Clinical manifestations include headache, nausea, emesis, seizures, altered mental status (in some cases progressing to coma), papilledema, and retinal hemorrhage. Focal neurologic signs may develop. Pathologically, this condition may be associated with the formation of ischemic lesions in the brain (brain ischemia). [NIH]

Hyperthyroidism: Excessive functional activity of the thyroid gland. [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]

Hypesthesia: Absent or reduced sensitivity to cutaneous stimulation. [NIH]

Hypnotic: A drug that acts to induce sleep. [EU]

Hypoglycemia: Abnormally low blood sugar [NIH]

Hypotension: Abnormally low blood pressure. [NIH]

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]

**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]

**Ibuprofen:** A nonsteroidal anti-inflammatory agent with analgesic properties used in the therapy of rheumatism and arthritis. [NIH]

**Ice Cream:** A frozen dairy food made from cream or butterfat, milk, sugar, and flavorings. Frozen custard and French-type ice creams also contain eggs. [NIH]

**Id:** The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Idiopathic: Describes a disease of unknown cause. [NIH]

Ileum: The lower end of the small intestine. [NIH]

Illusion: A false interpretation of a genuine percept. [NIH]

**Imipramine:** The prototypical tricyclic antidepressant. It has been used in major depression, dysthymia, bipolar depression, attention-deficit disorders, agoraphobia, and panic disorders. It has less sedative effect than some other members of this therapeutic group. [NIH]

**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]

**Immunity:** Nonsusceptibility to the invasive or pathogenic effects of foreign microorganisms or to the toxic effect of antigenic substances. [NIH]

**Immunization:** Deliberate stimulation of the host's immune response. Active immunization involves administration of antigens or immunologic adjuvants. Passive immunization
involves administration of immune sera or lymphocytes or their extracts (e.g., transfer factor, immune RNA) or transplantation of immunocompetent cell producing tissue (thymus or bone marrow). [NIH]

Immunodeficiency: The decreased ability of the body to fight infection and disease. [NIH]

**Immunodeficiency syndrome:** The inability of the body to produce an immune response. [NIH]

Immunogenic: Producing immunity; evoking an immune response. [EU]

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]

Immunosuppressive: Describes the ability to lower immune system responses. [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]

Incision: A cut made in the body during surgery. [NIH]

Incisor: Anything adapted for cutting; any one of the four front teeth in each jaw. [NIH]

**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]

**Indigestion:** Poor digestion. Symptoms include heartburn, nausea, bloating, and gas. Also called dyspepsia. [NIH]

**Indomethacin:** A non-steroidal anti-inflammatory agent (NSAID) that inhibits the enzyme cyclooxygenase necessary for the formation of prostaglandins and other autacoids. It also inhibits the motility of polymorphonuclear leukocytes. [NIH]

**Induction:** The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

**Infarction:** A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

**Infection:** 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local

infection may persist and spread by extension to become an acute, subacute, or chronic clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

**Infection Control:** Programs of disease surveillance, generally within health care facilities, designed to investigate, prevent, and control the spread of infections and their causative microorganisms. [NIH]

**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]

**Infiltration:** The diffusion or accumulation in a tissue or cells of substances not normal to it or in amounts of the normal. Also, the material so accumulated. [EU]

**Inflammation:** A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

**Inflammatory bowel disease:** A general term that refers to the inflammation of the colon and rectum. Inflammatory bowel disease includes ulcerative colitis and Crohn's disease. [NIH]

**Influenza:** An acute viral infection involving the respiratory tract. It is marked by inflammation of the nasal mucosa, the pharynx, and conjunctiva, and by headache and severe, often generalized, myalgia. [NIH]

**Infusion:** A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

**Ingestion:** Taking into the body by mouth [NIH]

Inhalation: The drawing of air or other substances into the lungs. [EU]

**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]

**Innervation:** 1. The distribution or supply of nerves to a part. 2. The supply of nervous energy or of nerve stimulus sent to a part. [EU]

**Inorganic:** Pertaining to substances not of organic origin. [EU]

Inotropic: Affecting the force or energy of muscular contractions. [EU]

**Insight:** The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Insomnia: Difficulty in going to sleep or getting enough sleep. [NIH]

Instillation: . [EU]

**Insulator:** Material covering the metal conductor of the lead. It is usually polyurethane or silicone. [NIH]

**Insulin:** A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

**Insulin-dependent diabetes mellitus:** A disease characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Autoimmune, genetic, and environmental factors are involved in the development of type I diabetes. [NIH]

Interleukin-1: A soluble factor produced by monocytes, macrophages, and other cells which

activates T-lymphocytes and potentiates their response to mitogens or antigens. IL-1 consists of two distinct forms, IL-1 alpha and IL-1 beta which perform the same functions but are distinct proteins. The biological effects of IL-1 include the ability to replace macrophage requirements for T-cell activation. The factor is distinct from interleukin-2. [NIH]

**Interleukin-2:** Chemical mediator produced by activated T lymphocytes and which regulates the proliferation of T cells, as well as playing a role in the regulation of NK cell activity. [NIH]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

**Internal Medicine:** A medical specialty concerned with the diagnosis and treatment of diseases of the internal organ systems of adults. [NIH]

**Interneurons:** Most generally any neurons which are not motor or sensory. Interneurons may also refer to neurons whose axons remain within a particular brain region as contrasted with projection neurons which have axons projecting to other brain regions. [NIH]

Interpersonal Relations: The reciprocal interaction of two or more persons. [NIH]

Intervertebral: Situated between two contiguous vertebrae. [EU]

**Intervertebral Disk Displacement:** An intervertebral disk in which the nucleus pulposus has protruded through surrounding fibrocartilage. This occurs most frequently in the lower lumbar region. [NIH]

Intestinal: Having to do with the intestines. [NIH]

Intestinal Flora: The bacteria, yeasts, and fungi that grow normally in the intestines. [NIH]

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

Intoxication: Poisoning, the state of being poisoned. [EU]

Intracellular: Inside a cell. [NIH]

Intracranial Embolism: The sudden obstruction of a blood vessel by an embolus. [NIH]

**Intracranial Embolism and Thrombosis:** Embolism or thrombosis involving blood vessels which supply intracranial structures. Emboli may originate from extracranial or intracranial sources. Thrombosis may occur in arterial or venous structures. [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]

**Intracranial Hypotension:** A condition in which there is a diminution or loss of muscular tonicity, in consequence of which the muscles may be stretched beyond their normal limits. [NIH]

**Intracranial Pressure:** Pressure within the cranial cavity. It is influenced by brain mass, the circulatory system, CSF dynamics, and skull rigidity. [NIH]

Intramuscular: IM. Within or into muscle. [NIH]

**Intrathecal:** Describes the fluid-filled space between the thin layers of tissue that cover the brain and spinal cord. Drugs can be injected into the fluid or a sample of the fluid can be removed for testing. [NIH]

Intravenous: IV. Into a vein. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

**Intubation:** Introduction of a tube into a hollow organ to restore or maintain patency if obstructed. It is differentiated from catheterization in that the insertion of a catheter is usually performed for the introducing or withdrawing of fluids from the body. [NIH]

**Invasive:** 1. Having the quality of invasiveness. 2. Involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Invertebrates: Animals that have no spinal column. [NIH]

Involuntary: Reaction occurring without intention or volition. [NIH]

**Iodine:** A nonmetallic element of the halogen group that is represented by the atomic symbol I, atomic number 53, and atomic weight of 126.90. It is a nutritionally essential element, especially important in thyroid hormone synthesis. In solution, it has anti-infective properties and is used topically. [NIH]

**Ion Channels:** Gated, ion-selective glycoproteins that traverse membranes. The stimulus for channel gating can be a membrane potential, drug, transmitter, cytoplasmic messenger, or a mechanical deformation. Ion channels which are integral parts of ionotropic neurotransmitter receptors are not included. [NIH]

**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]

Ipsilateral: Having to do with the same side of the body. [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]

**Irrigation:** The washing of a body cavity or surface by flowing solution which is inserted and then removed. Any drug in the irrigation solution may be absorbed. [NIH]

**Irritable Bowel Syndrome:** A disorder that comes and goes. Nerves that control the muscles in the GI tract are too active. The GI tract becomes sensitive to food, stool, gas, and stress. Causes abdominal pain, bloating, and constipation or diarrhea. Also called spastic colon or mucous colitis. [NIH]

**Irritants:** Drugs that act locally on cutaneous or mucosal surfaces to produce inflammation; those that cause redness due to hyperemia are rubefacients; those that raise blisters are vesicants and those that penetrate sebaceous glands and cause abscesses are pustulants; tear gases and mustard gases are also irritants. [NIH]

**Ischemia:** Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel. [EU]

**Ischemic stroke:** A condition in which the blood supply to part of the brain is cut off. Also called "plug-type" strokes. Blocked arteries starve areas of the brain controlling sight, speech, sensation, and movement so that these functions are partially or completely lost. Ischemic stroke is the most common type of stroke, accounting for 80 percent of all strokes. Most ischemic strokes are caused by a blood clot called a thrombus, which blocks blood flow in the arteries feeding the brain, usually the carotid artery in the neck, the major vessel bringing blood to the brain. When it becomes blocked, the risk of stroke is very high. [NIH]

**Isometric Contraction:** Muscular contractions characterized by increase in tension without change in length. [NIH]

**Jejunum:** That portion of the small intestine which extends from the duodenum to the ileum; called also intestinum jejunum. [EU]

**Jet lag:** Symptoms produced in human beings by fast travel through large meridian difference. [NIH]

**Joint:** The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

Kainate: Glutamate receptor. [NIH]

**Kaposi:** A tumor characterized by development, essentially in men, of violet red patches and nodules on the skin. This disease also affects deeper organs. [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]

**Ketamine:** A cyclohexanone derivative used for induction of anesthesia. Its mechanism of action is not well understood, but ketamine can block NMDA receptors (receptors, N-Methyl-D-Aspartate) and may interact with sigma receptors. [NIH]

**Ketanserin:** A selective serotonin receptor antagonist with weak adrenergic receptor blocking properties. The drug is effective in lowering blood pressure in essential hypertension. It also inhibits platelet aggregation. It is well tolerated and is particularly effective in older patients. [NIH]

**Ketone Bodies:** Chemicals that the body makes when there is not enough insulin in the blood and it must break down fat for its energy. Ketone bodies can poison and even kill body cells. When the body does not have the help of insulin, the ketones build up in the blood and then "spill" over into the urine so that the body can get rid of them. The body can also rid itself of one type of ketone, called acetone, through the lungs. This gives the breath a fruity odor. Ketones that build up in the body for a long time lead to serious illness and coma. [NIH]

**Kidney Disease:** Any one of several chronic conditions that are caused by damage to the cells of the kidney. People who have had diabetes for a long time may have kidney damage. Also called nephropathy. [NIH]

**Kidney stone:** A stone that develops from crystals that form in urine and build up on the inner surfaces of the kidney, in the renal pelvis, or in the ureters. [NIH]

Kinetics: The study of rate dynamics in chemical or physical systems. [NIH]

**Labile:** 1. Gliding; moving from point to point over the surface; unstable; fluctuating. 2. Chemically unstable. [EU]

**Labyrinth:** The internal ear; the essential part of the organ of hearing. It consists of an osseous and a membranous portion. [NIH]

Lactation: The period of the secretion of milk. [EU]

Lag: The time elapsing between application of a stimulus and the resulting reaction. [NIH]

**Laminin:** Large, noncollagenous glycoprotein with antigenic properties. It is localized in the basement membrane lamina lucida and functions to bind epithelial cells to the basement membrane. Evidence suggests that the protein plays a role in tumor invasion. [NIH]

**Large Intestine:** The part of the intestine that goes from the cecum to the rectum. The large intestine absorbs water from stool and changes it from a liquid to a solid form. The large intestine is 5 feet long and includes the appendix, cecum, colon, and rectum. Also called colon. [NIH]

Laryngeal: Having to do with 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]

**Lateral Ventricles:** Cavity in each of the cerebral hemispheres derived from the cavity of the embryonic neural tube. They are separated from each other by the septum pellucidum, and each communicates with the third ventricle by the foramen of Monro, through which also the choroid plexuses of the lateral ventricles become continuous with that of the third ventricle. [NIH]

**Laterality:** Behavioral manifestations of cerebral dominance in which there is preferential use and superior functioning of either the left or the right side, as in the preferred use of the right hand or right foot. [NIH]

**Lathyrism:** A paralytic condition of the legs caused by ingestion of lathyrogens, especially beta-aminopropionitrile, found in the seeds of plants of the genus Lathyrus. [NIH]

**Laxative:** An agent that acts to promote evacuation of the bowel; a cathartic or purgative. [EU]

**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]

**Leprosy:** A chronic granulomatous infection caused by Mycobacterium leprae. The granulomatous lesions are manifested in the skin, the mucous membranes, and the peripheral nerves. Two polar or principal types are lepromatous and tuberculoid. [NIH]

**Leptin:** A 16-kD peptide hormone secreted from white adipocytes and implicated in the regulation of food intake and energy balance. Leptin provides the key afferent signal from fat cells in the feedback system that controls body fat stores. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Lethargy: Abnormal drowsiness or stupor; a condition of indifference. [EU]

Leukemia: Cancer of blood-forming tissue. [NIH]

**Leukocytes:** White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

**Leukoplakia:** A white patch that may develop on mucous membranes such as the cheek, gums, or tongue and may become cancerous. [NIH]

**Levorphanol:** A narcotic analgesic that may be habit-forming. It is nearly as effective orally as by injection. [NIH]

**Libido:** The psychic drive or energy associated with sexual instinct in the broad sense (pleasure and love-object seeking). It may also connote the psychic energy associated with instincts in general that motivate behavior. [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]

**Light microscope:** A microscope (device to magnify small objects) in which objects are lit directly by white light. [NIH]

Lincomycin:(2S-trans)-Methyl6,8-dideoxy-6-(((1-methyl-4-propyl-2-pyrrolidinyl)carbonyl)amino)-1-thio-D-erythro-alpha-D-galacto-octopyranoside.Anantibiotic produced by Streptomyces lincolnensis var.lincolnensis. It has been used in the<br/>treatment of staphylococcal, streptococcal, and Bacteroides fragilis infections. [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]

Lip: Either of the two fleshy, full-blooded margins of the mouth. [NIH]

Lipid: Fat. [NIH]

**Lipid A:** Lipid A is the biologically active component of lipopolysaccharides. It shows strong endotoxic activity and exhibits immunogenic properties. [NIH]

Lipopolysaccharides: Substance consisting of polysaccaride and lipid. [NIH]

**Lipoxygenase:** An enzyme of the oxidoreductase class that catalyzes reactions between linoleate and other fatty acids and oxygen to form hydroperoxy-fatty acid derivatives. Related enzymes in this class include the arachidonate lipoxygenases, arachidonate 5-lipoxygenase, arachidonate 12-lipoxygenase, and arachidonate 15-lipoxygenase. EC 1.13.11.12. [NIH]

**Lithium:** An element in the alkali metals family. It has the atomic symbol Li, atomic number 3, and atomic weight 6.94. Salts of lithium are used in treating manic-depressive disorders. [NIH]

**Liver:** A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

**Liver scan:** An image of the liver created on a computer screen or on film. A radioactive substance is injected into a blood vessel and travels through the bloodstream. It collects in the liver, especially in abnormal areas, and can be detected by the scanner. [NIH]

Lobe: A portion of an organ such as the liver, lung, breast, or brain. [NIH]

Local therapy: Treatment that affects cells in the tumor and the area close to it. [NIH]

**Localization:** The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

Localized: Cancer which has not metastasized yet. [NIH]

**Locomotion:** Movement or the ability to move from one place or another. It can refer to humans, vertebrate or invertebrate animals, and microorganisms. [NIH]

**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]

**Low Back Pain:** Acute or chronic pain in the lumbar or sacral regions, which may be associated with musculo-ligamentous sprains and strains; intervertebral disk displacement; and other conditions. [NIH]

Lubricants: Oily or slippery substances. [NIH]

**Lubrication:** The application of a substance to diminish friction between two surfaces. It may refer to oils, greases, and similar substances for the lubrication of medical equipment but it can be used for the application of substances to tissue to reduce friction, such as lotions for skin and vaginal lubricants. [NIH]

Lumbar: Pertaining to the loins, the part of the back between the thorax and the pelvis. [EU]

**Lumbar puncture:** A procedure in which a needle is put into the lower part of the spinal column to collect cerebrospinal fluid or to give anticancer drugs intrathecally. Also called a spinal tap. [NIH]

**Luminescence:** The property of giving off light without emitting a corresponding degree of heat. It includes the luminescence of inorganic matter or the bioluminescence of human

matter, invertebrates and other living organisms. For the luminescence of bacteria, bacterial luminescence is available. [NIH]

**Lupus:** A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

**Lymph:** The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

**Lymph node:** A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Also known as a lymph gland. Lymph nodes are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic fluid (lymph). [NIH]

**Lymphatic:** The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

**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]

Lymphocytosis: Excess of normal lymphocytes in the blood or in any effusion. [NIH]

**Lymphoid:** Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphoma: A general term for various neoplastic diseases of the lymphoid tissue. [NIH]

**Lysergic acid:** A compound close in chemical structure to LSD-25 but without hallucinogenic effects; one of the direct chemical predecessors of LSD-25. Sometimes LSD-25 is erroneously called by this name. [NIH]

**Lysergic Acid Diethylamide:** Semisynthetic derivative of ergot (Claviceps purpurea). It has complex effects on serotonergic systems including antagonism at some peripheral serotonin receptors, both agonist and antagonist actions at central nervous system serotonin receptors, and possibly effects on serotonin turnover. It is a potent hallucinogen, but the mechanisms of that effect are not well understood. [NIH]

Lysine: An essential amino acid. It is often added to animal feed. [NIH]

Lytic: 1. Pertaining to lysis or to a lysin. 2. Producing lysis. [EU]

**Macrophage:** A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells. [NIH]

**Magnesium Hydroxide:** Magnesium hydroxide (Mg(OH)2). An inorganic compound that occurs in nature as the mineral brucite. It acts as an antacid with cathartic effects. [NIH]

**Magnesium Oxide:** Magnesium oxide (MgO). An inorganic compound that occurs in nature as the mineral periclase. In aqueous media combines quickly with water to form magnesium hydroxide. It is used as an antacid and mild laxative and has many nonmedicinal uses. [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]

**Magnetic Resonance Spectroscopy:** Spectroscopic method of measuring the magnetic moment of elementary particles such as atomic nuclei, protons or electrons. It is employed in clinical applications such as NMR Tomography (magnetic resonance imaging). [NIH]

**Maintenance therapy:** Treatment that is given to help a primary (original) treatment keep working. Maintenance therapy is often given to help keep cancer in remission. [NIH]

**Malabsorption:** Impaired intestinal absorption of nutrients. [EU]

Malaise: A vague feeling of bodily discomfort. [EU]

**Malaria:** A protozoan disease caused in humans by four species of the genus Plasmodium (P. falciparum (malaria, falciparum), P. vivax (malaria, vivax), P. ovale, and P. malariae) and transmitted by the bite of an infected female mosquito of the genus Anopheles. Malaria is endemic in parts of Asia, Africa, Central and South America, Oceania, and certain Caribbean islands. It is characterized by extreme exhaustion associated with paroxysms of high fever, sweating, shaking chills, and anemia. Malaria in animals is caused by other species of plasmodia. [NIH]

**Malaria**, **Falciparum**: Malaria caused by Plasmodium falciparum. This is the severest form of malaria and is associated with the highest levels of parasites in the blood. This disease is characterized by irregularly recurring febrile paroxysms that in extreme cases occur with acute cerebral, renal, or gastrointestinal manifestations. [NIH]

**Malaria**, **Vivax:** Malaria caused by Plasmodium vivax. This form of malaria is less severe than malaria, falciparum, but there is a higher probability for relapses to occur. Febrile paroxysms often occur every other day. [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]

**Malnutrition:** A condition caused by not eating enough food or not eating a balanced diet. [NIH]

Mammary: Pertaining to the mamma, or breast. [EU]

Mammogram: An x-ray of the breast. [NIH]

**Mandible:** The largest and strongest bone of the face constituting the lower jaw. It supports the lower teeth. [NIH]

**Mandibular Nerve:** A branch of the trigeminal (5th cranial) nerve. The mandibular nerve carries motor fibers to the muscles of mastication and sensory fibers to the teeth and gingivae, the face in the region of the mandible, and parts of the dura. [NIH]

**Mania:** Excitement of psychotic proportions manifested by mental and physical hyperactivity, disorganization of behaviour, and elevation of mood. [EU]

Manic: Affected with mania. [EU]

**Manic-depressive psychosis:** One of a group of psychotic reactions, fundamentally marked by severe mood swings and a tendency to remission and recurrence. [NIH]

**Manifest:** Being the part or aspect of a phenomenon that is directly observable : concretely expressed in behaviour. [EU]

Mannans: Polysaccharides consisting of mannose units. [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]

**Maxillary Nerve:** The intermediate sensory division of the trigeminal (5th cranial) nerve. The maxillary nerve carries general afferents from the intermediate region of the face

including the lower eyelid, nose and upper lip, the maxillary teeth, and parts of the dura. [NIH]

**Meat:** The edible portions of any animal used for food including domestic mammals (the major ones being cattle, swine, and sheep) along with poultry, fish, shellfish, and game. [NIH]

Medial: Lying near the midsaggital plane of the body; opposed to lateral. [NIH]

**Median Nerve:** A major nerve of the upper extremity. In humans, the fibers of the median nerve originate in the lower cervical and upper thoracic spinal cord (usually C6 to T1), travel via the brachial plexus, and supply sensory and motor innervation to parts of the forearm and hand. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

**Mediator:** An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

**Medical Records:** Recording of pertinent information concerning patient's illness or illnesses. [NIH]

**Medical Staff:** Professional medical personnel who provide care to patients in an organized facility, institution or agency. [NIH]

Medicament: A medicinal substance or agent. [EU]

**MEDLINE:** An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Medullary: Pertaining to the marrow or to any medulla; resembling marrow. [EU]

**Meiosis:** A special method of cell division, occurring in maturation of the germ cells, by means of which each daughter nucleus receives half the number of chromosomes characteristic of the somatic cells of the species. [NIH]

**Melanocytes:** Epidermal dendritic pigment cells which control long-term morphological color changes by alteration in their number or in the amount of pigment they produce and store in the pigment containing organelles called melanosomes. Melanophores are larger cells which do not exist in mammals. [NIH]

**Melanoma:** A form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

Membrane Glycoproteins: Glycoproteins found on the membrane or surface of cells. [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]

Meningeal: Refers to the meninges, the tissue covering the brain and spinal cord. [NIH]

Meninges: The three membranes that cover and protect the brain and spinal cord. [NIH]

**Meningitis:** Inflammation of the meninges. When it affects the dura mater, the disease is termed pachymeningitis; when the arachnoid and pia mater are involved, it is called leptomeningitis, or meningitis proper. [EU]

Menopause: Permanent cessation of menstruation. [NIH]

Menstrual Cycle: The period of the regularly recurring physiologic changes in the

endometrium occurring during the reproductive period in human females and some primates and culminating in partial sloughing of the endometrium (menstruation). [NIH]

**Menstruation:** The normal physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus. [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]

Menthol: An alcohol produced from mint oils or prepared synthetically. [NIH]

**Meperidine:** 1-Methyl-4-phenyl-4-piperidinecarboxylic acid ethyl ester. A narcotic analgesic that can be used for the relief of most types of moderate to severe pain, including postoperative pain and the pain of labor. Prolonged use may lead to dependence of the morphine type; withdrawal symptoms appear more rapidly than with morphine and are of shorter duration. [NIH]

**Meta-Analysis:** A quantitative method of combining the results of independent studies (usually drawn from the published literature) and synthesizing summaries and conclusions which may be used to evaluate therapeutic effectiveness, plan new studies, etc., with application chiefly in the areas of research and medicine. [NIH]

Metabolite: Any substance produced by metabolism or by a metabolic process. [EU]

**Metabotropic:** A glutamate receptor which triggers an increase in production of 2 intracellular messengers: diacylglycerol and inositol 1, 4, 5-triphosphate. [NIH]

**Metastasis:** The spread of cancer from one part of the body to another. Tumors formed from cells that have spread are called "secondary tumors" and contain cells that are like those in the original (primary) tumor. The plural is metastases. [NIH]

**Metastatic:** Having to do with metastasis, which is the spread of cancer from one part of the body to another. [NIH]

**Methionine:** A sulfur containing essential amino acid that is important in many body functions. It is a chelating agent for heavy metals. [NIH]

**Methysergide:** An ergot derivative that is a congener of lysergic acid diethylamide. It antagonizes the effects of serotonin in blood vessels and gastrointestinal smooth muscle, but has few of the properties of other ergot alkaloids. Methysergide is used prophylactically in migraine and other vascular headaches and to antagonize serotonin in the carcinoid syndrome. [NIH]

Metoclopramide: A dopamine D2 antagonist that is used as an antiemetic. [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]

**Microbiological:** Pertaining to microbiology : the science that deals with microorganisms, including algae, bacteria, fungi, protozoa and viruses. [EU]

**Microbiology:** The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

**Microcalcifications:** Tiny deposits of calcium in the breast that cannot be felt but can be detected on a mammogram. A cluster of these very small specks of calcium may indicate

that cancer is present. [NIH]

**Microorganism:** An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

**Microscopy:** The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

**Middle Cerebral Artery:** The largest and most complex of the cerebral arteries. Branches of the middle cerebral artery supply the insular region, motor and premotor areas, and large regions of the association cortex. [NIH]

**Migrans:** Infestation of the dermis by various larvae, characterized by bizarre red irregular lines which are broad at one end and fade at the other, produced by burrowing larvae. [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]

Mitotic: Cell resulting from mitosis. [NIH]

**Mobilization:** The process of making a fixed part or stored substance mobile, as by separating a part from surrounding structures to make it accessible for an operative procedure or by causing release into the circulation for body use of a substance stored in the body. [EU]

**Modeling:** A treatment procedure whereby the therapist presents the target behavior which the learner is to imitate and make part of his repertoire. [NIH]

**Modification:** A change in an organism, or in a process in an organism, that is acquired from its own activity or environment. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

**Molecular Structure:** The location of the atoms, groups or ions relative to one another in a molecule, as well as the number, type and location of covalent bonds. [NIH]

**Molecule:** A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

**Monitor:** An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

**Monoclonal:** An antibody produced by culturing a single type of cell. It therefore consists of a single species of immunoglobulin molecules. [NIH]

**Monocytes:** Large, phagocytic mononuclear leukocytes produced in the vertebrate bone marrow and released into the blood; contain a large, oval or somewhat indented nucleus surrounded by voluminous cytoplasm and numerous organelles. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

**Morphine:** The principal alkaloid in opium and the prototype opiate analgesic and narcotic. Morphine has widespread effects in the central nervous system and on smooth muscle. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Motility: The ability to move spontaneously. [EU]

**Motion Sickness:** Sickness caused by motion, as sea sickness, train sickness, car sickness, and air sickness. [NIH]

Motor Activity: The physical activity of an organism as a behavioral phenomenon. [NIH]

**Motor Cortex:** Area of the frontal lobe concerned with primary motor control. It lies anterior to the central sulcus. [NIH]

Mucinous: Containing or resembling mucin, the main compound in mucus. [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]

**Mucus:** The viscous secretion of mucous membranes. It contains mucin, white blood cells, water, inorganic salts, and exfoliated cells. [NIH]

**Multiple sclerosis:** A disorder of the central nervous system marked by weakness, numbness, a loss of muscle coordination, and problems with vision, speech, and bladder control. Multiple sclerosis is thought to be an autoimmune disease in which the body's immune system destroys myelin. Myelin is a substance that contains both protein and fat (lipid) and serves as a nerve insulator and helps in the transmission of nerve signals. [NIH]

**Muscle Contraction:** A process leading to shortening and/or development of tension in muscle tissue. Muscle contraction occurs by a sliding filament mechanism whereby actin filaments slide inward among the myosin filaments. [NIH]

**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]

**Muscle Relaxation:** That phase of a muscle twitch during which a muscle returns to a resting position. [NIH]

**Muscle tension:** A force in a material tending to produce extension; the state of being stretched. [NIH]

**Muscular Atrophy:** Derangement in size and number of muscle fibers occurring with aging, reduction in blood supply, or following immobilization, prolonged weightlessness, malnutrition, and particularly in denervation. [NIH]

**Muscular Dystrophies:** A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

**Mustard Gas:** Severe irritant and vesicant of skin, eyes, and lungs. It may cause blindness and lethal lung edema and was formerly used as a war gas. The substance has been proposed as a cytostatic and for treatment of psoriasis. It has been listed as a known carcinogen in the Fourth Annual Report on Carcinogens (NTP-85-002, 1985) (Merck, 11th ed). [NIH]

Myalgia: Pain in a muscle or muscles. [EU]

Mydriatic: 1. Dilating the pupil. 2. Any drug that dilates the pupil. [EU]

Myelin: The fatty substance that covers and protects nerves. [NIH]

**Myelography:** X-ray visualization of the spinal cord following injection of contrast medium into the spinal arachnoid space. [NIH]

**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]

**Myocardium:** The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myopathy: Any disease of a muscle. [EU]

**Myopia:** That error of refraction in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina, as a result of the eyeball being too long from front to back (axial m.) or of an increased strength in refractive power of the media of the eye (index m.). Called also nearsightedness, because the near point is less distant than it is in emmetropia with an equal amplitude of accommodation. [EU]

**Myosin:** Chief protein in muscle and the main constituent of the thick filaments of muscle fibers. In conjunction with actin, it is responsible for the contraction and relaxation of muscles. [NIH]

**Myotonic Dystrophy:** A condition presenting muscle weakness and wasting which may be progressive. [NIH]

**Naloxone:** A specific opiate antagonist that has no agonist activity. It is a competitive antagonist at mu, delta, and kappa opioid receptors. [NIH]

**Naltrexone:** Derivative of noroxymorphone that is the N-cyclopropylmethyl congener of naloxone. It is a narcotic antagonist that is effective orally, longer lasting and more potent than naloxone, and has been proposed for the treatment of heroin addiction. The FDA has approved naltrexone for the treatment of alcohol dependence. [NIH]

**Narcosis:** A general and nonspecific reversible depression of neuronal excitability, produced by a number of physical and chemical aspects, usually resulting in stupor. [NIH]

**Narcotic:** 1. Pertaining to or producing narcosis. 2. An agent that produces insensibility or stupor, applied especially to the opioids, i.e. to any natural or synthetic drug that has morphine-like actions. [EU]

**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 Lavage Fluid:** Fluid obtained by irrigation or washout of the nasal cavity and nasal mucosa. The resulting fluid is used in cytologic and immunologic assays of the nasal mucosa such as with the nasal provocation test in the diagnosis of nasal hypersensitivity. [NIH]

Nasal Mucosa: The mucous membrane lining the nasal cavity. [NIH]

**Nasal Obstruction:** Any hindrance to the passage of air into and out of the nose. The obstruction may be in the nasal vestibule, fossae, or other areas of the nasal cavity. [NIH]

**Nasal Septum:** The partition separating the two nasal cavities in the midplane, composed of cartilaginous, membranous and bony parts. [NIH]

**Nausea:** An unpleasant sensation in the stomach usually accompanied by the urge to vomit. Common causes are early pregnancy, sea and motion sickness, emotional stress, intense pain, food poisoning, and various enteroviruses. [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]

Nearsightedness: The common term for myopia. [NIH]

**Neck Injuries:** General or unspecified injuries to the neck. It includes injuries to the skin, muscles, and other soft tissues of the neck. [NIH]

Neck Muscles: The neck muscles consist of the platysma, splenius cervicis, sternocleidomastoid(eus), longus colli, the anterior, medius, and posterior scalenes,

digastric(us), stylohyoid(eus), mylohyoid(eus), geniohyoid(eus), sternohyoid(eus), omohyoid(eus), sternothyroid(eus), and thyrohyoid(eus). [NIH]

**Neck Pain:** Discomfort or more intense forms of pain that are localized to the cervical region. This term generally refers to pain in the posterior or lateral regions of the neck. [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]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

**Neoplasm:** A new growth of benign or malignant tissue. [NIH]

**Neoplastic:** Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Nephropathy: Disease of the kidneys. [EU]

**Nerve:** A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

**Nerve Endings:** Specialized terminations of peripheral neurons. Nerve endings include neuroeffector junction(s) by which neurons activate target organs and sensory receptors which transduce information from the various sensory modalities and send it centrally in the nervous system. Presynaptic nerve endings are presynaptic terminals. [NIH]

**Nerve Fibers:** Slender processes of neurons, especially the prolonged axons that conduct nerve impulses. [NIH]

**Nerve Growth Factor:** Nerve growth factor is the first of a series of neurotrophic factors that were found to influence the growth and differentiation of sympathetic and sensory neurons. It is comprised of alpha, beta, and gamma subunits. The beta subunit is responsible for its growth stimulating activity. [NIH]

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

Nervousness: Excessive excitability and irritability, with mental and physical unrest. [EU]

**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 Pathways:** Neural tracts connecting one part of the nervous system with another. [NIH]

**Neuralgia:** Intense or aching pain that occurs along the course or distribution of a peripheral or cranial nerve. [NIH]

**Neurasthenia:** A mental disorder characterized by chronic fatigue and concomitant physiologic symptoms. [NIH]

**Neuritis:** A general term indicating inflammation of a peripheral or cranial nerve. Clinical manifestation may include pain; paresthesias; paresis; or hypesthesia. [NIH]

**Neuroanatomy:** Study of the anatomy of the nervous system as a specialty or discipline. [NIH]

**Neurodegenerative Diseases:** Hereditary and sporadic conditions which are characterized by progressive nervous system dysfunction. These disorders are often associated with

atrophy of the affected central or peripheral nervous system structures. [NIH]

**Neuroeffector Junction:** The synapse between a neuron (presynaptic) and an effector cell other than another neuron (postsynaptic). Neuroeffector junctions include synapses onto muscles and onto secretory cells. [NIH]

**Neuroendocrine:** Having to do with the interactions between the nervous system and the endocrine system. Describes certain cells that release hormones into the blood in response to stimulation of the nervous system. [NIH]

**Neurogenic:** Loss of bladder control caused by damage to the nerves controlling the bladder. [NIH]

**Neurogenic Inflammation:** Inflammation caused by an injurious stimulus of peripheral neurons and resulting in release of neuropeptides which affect vascular permeability and help initiate proinflammatory and immune reactions at the site of injury. [NIH]

**Neuroleptic:** A term coined to refer to the effects on cognition and behaviour of antipsychotic drugs, which produce a state of apathy, lack of initiative, and limited range of emotion and in psychotic patients cause a reduction in confusion and agitation and normalization of psychomotor activity. [EU]

Neurologic: Having to do with nerves or the nervous system. [NIH]

**Neurologist:** A doctor who specializes in the diagnosis and treatment of disorders of the nervous system. [NIH]

**Neurology:** A medical specialty concerned with the study of the structures, functions, and diseases of the nervous system. [NIH]

Neuroma: A tumor that arises in nerve cells. [NIH]

Neuromuscular: Pertaining to muscles and nerves. [EU]

Neuromuscular Junction: The synapse between a neuron and a muscle. [NIH]

**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]

**Neuropathy:** A problem in any part of the nervous system except the brain and spinal cord. Neuropathies can be caused by infection, toxic substances, or disease. [NIH]

**Neuropeptide:** A member of a class of protein-like molecules made in the brain. Neuropeptides consist of short chains of amino acids, with some functioning as neurotransmitters and some functioning as hormones. [NIH]

**Neuroprotective Agents:** Drugs intended to prevent damage to the brain or spinal cord from ischemia, stroke, convulsions, or trauma. Some must be administered before the event, but others may be effective for some time after. They act by a variety of mechanisms, but often directly or indirectly minimize the damage produced by endogenous excitatory amino acids. [NIH]

Neuroretinitis: Inflammation of the optic nerve head and adjacent retina. [NIH]

**Neurosis:** Functional derangement due to disorders of the nervous system which does not affect the psychic personality of the patient. [NIH]

**Neurotic:** 1. Pertaining to or characterized by neurosis. 2. A person affected with a neurosis. [EU]

**Neurotoxicity:** The tendency of some treatments to cause damage to the nervous system. [NIH]

Neurotoxin: A substance that is poisonous to nerve tissue. [NIH]

**Neurotransmitters:** Endogenous signaling molecules that alter the behavior of neurons or effector cells. Neurotransmitter is used here in its most general sense, including not only messengers that act directly to regulate ion channels, but also those that act through second messenger systems, and those that act at a distance from their site of release. Included are neuromodulators, neuroregulators, neuromediators, and neurohumors, whether or not acting at synapses. [NIH]

**Neutrons:** Electrically neutral elementary particles found in all atomic nuclei except light hydrogen; the mass is equal to that of the proton and electron combined and they are unstable when isolated from the nucleus, undergoing beta decay. Slow, thermal, epithermal, and fast neutrons refer to the energy levels with which the neutrons are ejected from heavier nuclei during their decay. [NIH]

**Neutrophils:** Granular leukocytes having a nucleus with three to five lobes connected by slender threads of chromatin, and cytoplasm containing fine inconspicuous granules and stainable by neutral dyes. [NIH]

**Niacin:** Water-soluble vitamin of the B complex occurring in various animal and plant tissues. Required by the body for the formation of coenzymes NAD and NADP. Has pellagra-curative, vasodilating, and antilipemic properties. [NIH]

**Niacinamide:** An important compound functioning as a component of the coenzyme NAD. Its primary significance is in the prevention and/or cure of blacktongue and pellagra. Most animals cannot manufacture this compound in amounts sufficient to prevent nutritional deficiency and it therefore must be supplemented through dietary intake. [NIH]

**Nicotine:** Nicotine is highly toxic alkaloid. It is the prototypical agonist at nicotinic cholinergic receptors where it dramatically stimulates neurons and ultimately blocks synaptic transmission. Nicotine is also important medically because of its presence in tobacco smoke. [NIH]

**Nitrates:** Inorganic or organic salts and esters of nitric acid. These compounds contain the NO3- radical. [NIH]

**Nitric acid:** A toxic, corrosive, colorless liquid used to make fertilizers, dyes, explosives, and other chemicals. [NIH]

**Nitric Oxide:** A free radical gas produced endogenously by a variety of mammalian cells. It is synthesized from arginine by a complex reaction, catalyzed by nitric oxide synthase. Nitric oxide is endothelium-derived relaxing factor. It is released by the vascular endothelium and mediates the relaxation induced by some vasodilators such as acetylcholine and bradykinin. It also inhibits platelet aggregation, induces disaggregation of aggregated platelets, and inhibits platelet adhesion to the vascular endothelium. Nitric oxide activates cytosolic guanylate cyclase and thus elevates intracellular levels of cyclic GMP. [NIH]

**Nitrogen:** An element with the atomic symbol N, atomic number 7, and atomic weight 14. Nitrogen exists as a diatomic gas and makes up about 78% of the earth's atmosphere by volume. It is a constituent of proteins and nucleic acids and found in all living cells. [NIH]

**Nitroglycerin:** A highly volatile organic nitrate that acts as a dilator of arterial and venous smooth muscle and is used in the treatment of angina. It provides relief through improvement of the balance between myocardial oxygen supply and demand. Although total coronary blood flow is not increased, there is redistribution of blood flow in the heart when partial occlusion of coronary circulation is effected. [NIH]

**Norepinephrine:** Precursor of epinephrine that is secreted by the adrenal medulla and is a widespread central and autonomic neurotransmitter. Norepinephrine is the principal

transmitter of most postganglionic sympathetic fibers and of the diffuse projection system in the brain arising from the locus ceruleus. It is also found in plants and is used pharmacologically as a sympathomimetic. [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]

**Nucleus:** A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

**Observational study:** An epidemiologic study that does not involve any intervention, experimental or otherwise. Such a study may be one in which nature is allowed to take its course, with changes in one characteristic being studied in relation to changes in other characteristics. Analytical epidemiologic methods, such as case-control and cohort study designs, are properly called observational epidemiology because the investigator is observing without intervention other than to record, classify, count, and statistically analyze results. [NIH]

**Obstetrics:** A medical-surgical specialty concerned with management and care of women during pregnancy, parturition, and the puerperium. [NIH]

Occipital Lobe: Posterior part of the cerebral hemisphere. [NIH]

Occult: Obscure; concealed from observation, difficult to understand. [EU]

**Ocular:** 1. Of, pertaining to, or affecting the eye. 2. Eyepiece. [EU]

**Oculi:** Globe or ball of the eye. [NIH]

**Oculomotor:** Cranial nerve III. It originate from the lower ventral surface of the midbrain and is classified as a motor nerve. [NIH]

**Oculomotor Nerve:** The 3d cranial nerve. The oculomotor nerve sends motor fibers to the levator muscles of the eyelid and to the superior rectus, inferior rectus, and inferior oblique muscles of the eye. It also sends parasympathetic efferents (via the ciliary ganglion) to the muscles controlling pupillary constriction and accommodation. The motor fibers originate in the oculomotor nuclei of the midbrain. [NIH]

**Odds Ratio:** The ratio of two odds. The exposure-odds ratio for case control data is the ratio of the odds in favor of exposure among cases to the odds in favor of exposure among noncases. The disease-odds ratio for a cohort or cross section is the ratio of the odds in favor of disease among the exposed to the odds in favor of disease among the unexposed. The prevalence-odds ratio refers to an odds ratio derived cross-sectionally from studies of prevalent cases. [NIH]

Odour: A volatile emanation that is perceived by the sense of smell. [EU]

**Office Automation:** Use of computers or computer systems for doing routine clerical work, e.g., billing, records pertaining to the administration of the office, etc. [NIH]

**Office Visits:** Visits made by patients to health service providers' offices for diagnosis, treatment, and follow-up. [NIH]

Ointments: Semisolid preparations used topically for protective emollient effects or as a

vehicle for local administration of medications. Ointment bases are various mixtures of fats, waxes, animal and plant oils and solid and liquid hydrocarbons. [NIH]

**Oncogene:** A gene that normally directs cell growth. If altered, an oncogene can promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by an environmental exposure to carcinogens. [NIH]

On-line: A sexually-reproducing population derived from a common parentage. [NIH]

Oophorectomy: Surgery to remove one or both ovaries. [NIH]

Opacity: Degree of density (area most dense taken for reading). [NIH]

**Ophthalmic:** Pertaining to the eye. [EU]

**Opium:** The air-dried exudate from the unripe seed capsule of the opium poppy, Papaver somniferum, or its variant, P. album. It contains a number of alkaloids, but only a few - morphine, codeine, and papaverine - have clinical significance. Opium has been used as an analgesic, antitussive, antidiarrheal, and antispasmodic. [NIH]

**Opportunistic Infections:** An infection caused by an organism which becomes pathogenic under certain conditions, e.g., during immunosuppression. [NIH]

**Optic Chiasm:** The X-shaped structure formed by the meeting of the two optic nerves. At the optic chiasm the fibers from the medial part of each retina cross to project to the other side of the brain while the lateral retinal fibers continue on the same side. As a result each half of the brain receives information about the contralateral visual field from both eyes. [NIH]

**Optic Disk:** The portion of the optic nerve seen in the fundus with the ophthalmoscope. It is formed by the meeting of all the retinal ganglion cell axons as they enter the optic nerve. [NIH]

**Optic Nerve:** The 2nd cranial nerve. The optic nerve conveys visual information from the retina to the brain. The nerve carries the axons of the retinal ganglion cells which sort at the optic chiasm and continue via the optic tracts to the brain. The largest projection is to the lateral geniculate nuclei; other important targets include the superior colliculi and the suprachiasmatic nuclei. Though known as the second cranial nerve, it is considered part of the central nervous system. [NIH]

**Optic Nerve Diseases:** Conditions which produce injury or dysfunction of the second cranial or optic nerve, which is generally considered a component of the central nervous system. Damage to optic nerve fibers may occur at or near their origin in the retina, at the optic disk, or in the nerve, optic chiasm, optic tract, or lateral geniculate nuclei. Clinical manifestations may include decreased visual acuity and contrast sensitivity, impaired color vision, and an afferent pupillary defect. [NIH]

**Oral Health:** The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [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]

**Orbit:** One of the two cavities in the skull which contains an eyeball. Each eye is located in a bony socket or orbit. [NIH]

**Orbital:** Pertaining to the orbit (= the bony cavity that contains the eyeball). [EU]

**Organelles:** Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum; lysomomes; plastids; and vacuoles. [NIH]

**Orofacial:** Of or relating to the mouth and face. [EU]

Orthostatic: Pertaining to or caused by standing erect. [EU]

**Osteoarthritis:** Degeneration of articular cartilage. Primary osteoarthritis is very common in older persons, especially affecting weight-bearing joints. Articular cartilage becomes soft, frayed and thinned. [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]

**Outpatient:** A patient who is not an inmate of a hospital but receives diagnosis or treatment in a clinic or dispensary connected with the hospital. [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]

**Oxazoles:** Five-membered heterocyclic ring structures containing an oxygen in the 1-position and a nitrogen in the 3-position. [NIH]

**Oxygenation:** The process of supplying, treating, or mixing with oxygen. No:1245 - oxygenation the process of supplying, treating, or mixing with oxygen. [EU]

**Pachymeningitis:** Inflammation of the dura mater of the brain, the spinal cord or the optic nerve. [NIH]

**Pain Threshold:** Amount of stimulation required before the sensation of pain is experienced. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

**Palliative therapy:** Treatment given to relieve symptoms caused by advanced cancer. Palliative therapy does not alter the course of a disease but improves the quality of life. [NIH]

**Palpation:** Application of fingers with light pressure to the surface of the body to determine consistence of parts beneath in physical diagnosis; includes palpation for determining the outlines of organs. [NIH]

**Palsy:** Disease of the peripheral nervous system occurring usually after many years of increased lead absorption. [NIH]

**Pancreas:** A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Pancreatic: Having to do with the pancreas. [NIH]

Pancreatic cancer: Cancer of the pancreas, a salivary gland of the abdomen. [NIH]

**Pancreatic Polypeptide:** A 36-amino acid polypeptide with physiological regulatory functions. It is secreted by pancreatic tissue. Plasma pancreatic polypeptide increases after ingestion of food, with age, and in disease states. A lack of pancreatic polypeptide in the islets of Langerhans has been associated with the obese syndrome in rats and mice. [NIH]

**Pancreatitis:** Acute or chronic inflammation of the pancreas, which may be asymptomatic or symptomatic, and which is due to autodigestion of a pancreatic tissue by its own enzymes. It is caused most often by alcoholism or biliary tract disease; less commonly it may be associated with hyperlipaemia, hyperparathyroidism, abdominal trauma (accidental or operative injury), vasculitis, or uraemia. [EU]

**Panic:** A state of extreme acute, intense anxiety and unreasoning fear accompanied by disorganization of personality function. [NIH]

**Panic Disorder:** A type of anxiety disorder characterized by unexpected panic attacks that last minutes or, rarely, hours. Panic attacks begin with intense apprehension, fear or terror and, often, a feeling of impending doom. Symptoms experienced during a panic attack include dyspnea or sensations of being smothered; dizziness, loss of balance or faintness; choking sensations; palpitations or accelerated heart rate; shakiness; sweating; nausea or other form of abdominal distress; depersonalization or derealization; paresthesias; hot flashes or chills; chest discomfort or pain; fear of dying and fear of not being in control of oneself or going crazy. Agoraphobia may also develop. Similar to other anxiety disorders, it may be inherited as an autosomal dominant trait. [NIH]

Papilledema: Swelling around the optic disk. [NIH]

Paralysis: Loss of ability to move all or part of the body. [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]

**Parasite:** An animal or a plant that lives on or in an organism of another species and gets at least some of its nutrition from that other organism. [NIH]

**Parenteral:** Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, etc. [EU]

**Paresis:** A general term referring to a mild to moderate degree of muscular weakness, occasionally used as a synonym for paralysis (severe or complete loss of motor function). In the older literature, paresis often referred specifically to paretic neurosyphilis. "General paresis" and "general paralysis" may still carry that connotation. Bilateral lower extremity paresis is referred to as paraparesis. [NIH]

**Paresthesia:** Subjective cutaneous sensations (e.g., cold, warmth, tingling, pressure, etc.) that are experienced spontaneously in the absence of stimulation. [NIH]

Paroxysmal: Recurring in paroxysms (= spasms or seizures). [EU]

**Partial remission:** The shrinking, but not complete disappearance, of a tumor in response to therapy. Also called partial response. [NIH]

Particle: A tiny mass of material. [EU]

**Partnership Practice:** A voluntary contract between two or more doctors who may or may not share responsibility for the care of patients, with proportional sharing of profits and losses. [NIH]

**Patch:** A piece of material used to cover or protect a wound, an injured part, etc.: a patch over the eye. [NIH]

Pathogen: Any disease-producing microorganism. [EU]

**Pathogenesis:** The cellular events and reactions that occur in the development of disease. [NIH]

**Pathologic:** 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologies: The study of abnormality, especially the study of diseases. [NIH]

Pathophysiology: Altered functions in an individual or an organ due to disease. [NIH]

**Patient Education:** The teaching or training of patients concerning their own health needs. [NIH]

**Patient Satisfaction:** The degree to which the individual regards the health care service or product or the manner in which it is delivered by the provider as useful, effective, or beneficial. [NIH]

**Patient Selection:** Criteria and standards used for the determination of the appropriateness of the inclusion of patients with specific conditions in proposed treatment plans and the criteria used for the inclusion of subjects in various clinical trials and other research protocols. [NIH]

**Peer Group:** Group composed of associates of same species, approximately the same age, and usually of similar rank or social status. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Penicillin: An antibiotic drug used to treat infection. [NIH]

Pepsin: An enzyme made in the stomach that breaks down proteins. [NIH]

Peptic: Pertaining to pepsin or to digestion; related to the action of gastric juices. [EU]

**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]

**Percutaneous:** Performed through the skin, as injection of radiopacque material in radiological examination, or the removal of tissue for biopsy accomplished by a needle. [EU]

**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]

**Pericardium:** The fibroserous sac surrounding the heart and the roots of the great vessels. [NIH]

**Peridural:** Around or external to the dura mater. [EU]

**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]

**Perioperative:** Around the time of surgery; usually lasts from the time of going into the hospital or doctor's office for surgery until the time the patient goes home. [NIH]

**Perioperative Care:** Interventions to provide care prior to, during, and immediately after surgery. [NIH]

**Peripheral Nerves:** The nerves outside of the brain and spinal cord, including the autonomic, cranial, and spinal nerves. Peripheral nerves contain non-neuronal cells and connective tissue as well as axons. The connective tissue layers include, from the outside to the inside, the epineurium, the perineurium, and the endoneurium. [NIH]

**Peripheral Nervous System:** The nervous system outside of the brain and spinal cord. The peripheral nervous system has autonomic and somatic divisions. The autonomic nervous system includes the enteric, parasympathetic, and sympathetic subdivisions. The somatic nervous system includes the cranial and spinal nerves and their ganglia and the peripheral sensory receptors. [NIH]

**Peripheral Nervous System Diseases:** Diseases of the peripheral nerves external to the brain and spinal cord, which includes diseases of the nerve roots, ganglia, plexi, autonomic

nerves, sensory nerves, and motor nerves. [NIH]

**Peripheral Neuropathy:** Nerve damage, usually affecting the feet and legs; causing pain, numbness, or a tingling feeling. Also called "somatic neuropathy" or "distal sensory polyneuropathy." [NIH]

**Peripheral Vascular Disease:** Disease in the large blood vessels of the arms, legs, and feet. People who have had diabetes for a long time may get this because major blood vessels in their arms, legs, and feet are blocked and these limbs do not receive enough blood. The signs of PVD are aching pains in the arms, legs, and feet (especially when walking) and foot sores that heal slowly. Although people with diabetes cannot always avoid PVD, doctors say they have a better chance of avoiding it if they take good care of their feet, do not smoke, and keep both their blood pressure and diabetes under good control. [NIH]

Perivascular: Situated around a vessel. [EU]

**Pernicious:** Tending to a fatal issue. [EU]

**Pharmaceutical Solutions:** Homogeneous liquid preparations that contain one or more chemical substances dissolved, i.e., molecularly dispersed, in a suitable solvent or mixture of mutually miscible solvents. For reasons of their ingredients, method of preparation, or use, they do not fall into another group of products. [NIH]

**Pharmacodynamic:** Is concerned with the response of living tissues to chemical stimuli, that is, the action of drugs on the living organism in the absence of disease. [NIH]

**Pharmacokinetic:** The mathematical analysis of the time courses of absorption, distribution, and elimination of drugs. [NIH]

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]

Phenyl: Ingredient used in cold and flu remedies. [NIH]

**Phenylalanine:** An aromatic amino acid that is essential in the animal diet. It is a precursor of melanin, dopamine, noradrenalin, and thyroxine. [NIH]

**Phobias:** An exaggerated and invariably pathological dread of some specific type of stimulus or situation. [NIH]

**Phosphodiesterase:** Effector enzyme that regulates the levels of a second messenger, the cyclic GMP. [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]

**Phosphorylation:** The introduction of a phosphoryl group into a compound through the formation of an ester bond between the compound and a phosphorus moiety. [NIH]

**Photophobia:** Abnormal sensitivity to light. This may occur as a manifestation of eye diseases; migraine; subarachnoid hemorrhage; meningitis; and other disorders. Photophobia may also occur in association with depression and other mental disorders. [NIH]

**Photosensitization:** The development of abnormally heightened reactivity of the skin to sunlight. [EU]

**Physical Examination:** Systematic and thorough inspection of the patient for physical signs of disease or abnormality. [NIH]

**Physical Therapy:** The restoration of function and the prevention of disability following disease or injury with the use of light, heat, cold, water, electricity, ultrasound, and exercise. [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]

**Pigment:** A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes, and hair. [NIH]

**Pilot Projects:** Small-scale tests of methods and procedures to be used on a larger scale if the pilot study demonstrates that these methods and procedures can work. [NIH]

Pilot study: The initial study examining a new method or treatment. [NIH]

**Piperidines:** A family of hexahydropyridines. Piperidine itself is found in the pepper plant as the alkaloid piperine. [NIH]

**Pituitary Gland:** A small, unpaired gland situated in the sella turcica tissue. It is connected to the hypothalamus by a short stalk. [NIH]

**Placenta:** A highly vascular fetal organ through which the fetus absorbs oxygen and other nutrients and excretes carbon dioxide and other wastes. It begins to form about the eighth day of gestation when the blastocyst adheres to the decidua. [NIH]

**Plants:** Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

**Plaque:** A clear zone in a bacterial culture grown on an agar plate caused by localized destruction of bacterial cells by a bacteriophage. The concentration of infective virus in a fluid can be estimated by applying the fluid to a culture and counting the number of. [NIH]

**Plasma:** The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

**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]

**Platelet Aggregation:** The attachment of platelets to one another. This clumping together can be induced by a number of agents (e.g., thrombin, collagen) and is part of the mechanism leading to the formation of a thrombus. [NIH]

**Platelets:** A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called thrombocytes. [NIH]

**Platinum:** Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

**Plexus:** A network or tangle; a general term for a network of lymphatic vessels, nerves, or veins. [EU]

**Pneumocephalus:** Presence of air or gas within the intracranial cavity (e.g., epidural space, subdural space, intracerebral, etc.) which may result from traumatic injuries, fistulous tract formation, erosions of the skull from neoplasms or infection, neurosurgical procedures, and other conditions. [NIH]

**Poisoning:** A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

**Polycystic:** An inherited disorder characterized by many grape-like clusters of fluid-filled cysts that make both kidneys larger over time. These cysts take over and destroy working kidney tissue. PKD may cause chronic renal failure and end-stage renal disease. [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]

**Polysaccharide:** A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

**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]

**Postherpetic Neuralgia:** Variety of neuralgia associated with migraine in which pain is felt in or behind the eye. [NIH]

**Postmenopausal:** Refers to the time after menopause. Menopause is the time in a woman's life when menstrual periods stop permanently; also called "change of life." [NIH]

Postoperative: After surgery. [NIH]

**Postsynaptic:** Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

**Post-traumatic:** Occurring as a result of or after injury. [EU]

**Post-traumatic stress disorder:** A psychological disorder that develops in some individuals after a major traumatic experience such as war, rape, domestic violence, or accident. [NIH]

**Postural:** Pertaining to posture or position. [EU]

**Potassium:** An element that is in the alkali group of metals. It has an atomic symbol K, atomic number 19, and atomic weight 39.10. It is the chief cation in the intracellular fluid of muscle and other cells. Potassium ion is a strong electrolyte and it plays a significant role in the regulation of fluid volume and maintenance of the water-electrolyte balance. [NIH]

Potassium Channels: Cell membrane glycoproteins selective for potassium ions. [NIH]

**Potentiate:** A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [NIH]

**Potentiating:** A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [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]

**Precipitating Factors:** Factors associated with the definitive onset of a disease, illness, accident, behavioral response, or course of action. Usually one factor is more important or more obviously recognizable than others, if several are involved, and one may often be regarded as "necessary". Examples include exposure to specific disease; amount or level of an infectious organism, drug, or noxious agent, etc. [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]

**Predictive factor:** A situation or condition that may increase a person's risk of developing a certain disease or disorder. [NIH]

**Prednisolone:** A glucocorticoid with the general properties of the corticosteroids. It is the drug of choice for all conditions in which routine systemic corticosteroid therapy is indicated, except adrenal deficiency states. [NIH]

**Prednisone:** A synthetic anti-inflammatory glucocorticoid derived from cortisone. It is biologically inert and converted to prednisolone in the liver. [NIH]

Premenstrual: Occurring before menstruation. [EU]

**Premenstrual Syndrome:** A syndrome occurring most often during the last week of the menstrual cycle and ending soon after the onset of menses. Some of the symptoms are emotional instability, insomnia, headache, nausea, vomiting, abdominal distension, and painful breasts. [NIH]

**Pressoreceptors:** Receptors in the vascular system, particularly the aorta and carotid sinus, which are sensitive to stretch of the vessel walls. [NIH]

**Presynaptic:** Situated proximal to a synapse, or occurring before the synapse is crossed. [EU]

**Presynaptic Terminals:** The distal terminations of axons which are specialized for the release of neurotransmitters. Also included are varicosities along the course of axons which have similar specializations and also release transmitters. Presynaptic terminals in both the central and peripheral nervous systems are included. [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]

**Prion:** Small proteinaceous infectious particles that resist inactivation by procedures modifying nucleic acids and contain an abnormal isoform of a cellular protein which is a major and necessary component. [NIH]

Private Practice: Practice of a health profession by an individual, offering services on a

person-to-person basis, as opposed to group or partnership practice. [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]

**Projection:** A defense mechanism, operating unconsciously, whereby that which is emotionally unacceptable in the self is rejected and attributed (projected) to others. [NIH]

**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]

Prone: Having the front portion of the body downwards. [NIH]

**Prophase:** The first phase of cell division, in which the chromosomes become visible, the nucleus starts to lose its identity, the spindle appears, and the centrioles migrate toward opposite poles. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Propofol: A widely used anesthetic. [NIH]

**Propranolol:** A widely used non-cardioselective beta-adrenergic antagonist. Propranolol is used in the treatment or prevention of many disorders including acute myocardial infarction, arrhythmias, angina pectoris, hypertension, hypertensive emergencies, hyperthyroidism, migraine, pheochromocytoma, menopause, and anxiety. [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,  $\beta$ , 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]

**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]

**Prostatic Hyperplasia:** Enlargement or overgrowth of the prostate gland as a result of an increase in the number of its constituent cells. [NIH]

**Protective Agents:** Synthetic or natural substances which are given to prevent a disease or disorder or are used in the process of treating a disease or injury due to a poisonous agent. [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 Isoforms:** Different forms of a protein that may be produced from different genes, or from the same gene by alternative splicing. [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]

**Proteoglycan:** A molecule that contains both protein and glycosaminoglycans, which are a type of polysaccharide. Proteoglycans are found in cartilage and other connective tissues. [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]

**Prothrombin:** A plasma protein that is the inactive precursor of thrombin. It is converted to thrombin by a prothrombin activator complex consisting of factor Xa, factor V, phospholipid, and calcium ions. Deficiency of prothrombin leads to hypoprothrombinemia. [NIH]

**Protocol:** The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other aspects of trial design. [NIH]

**Protons:** Stable elementary particles having the smallest known positive charge, found in the nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

**Protozoa:** A subkingdom consisting of unicellular organisms that are the simplest in the animal kingdom. Most are free living. They range in size from submicroscopic to macroscopic. Protozoa are divided into seven phyla: Sarcomastigophora, Labyrinthomorpha, Apicomplexa, Microspora, Ascetospora, Myxozoa, and Ciliophora. [NIH]

Proximal: Nearest; closer to any point of reference; opposed to distal. [EU]

Pruritic: Pertaining to or characterized by pruritus. [EU]

**Psoriasis:** A common genetically determined, chronic, inflammatory skin disease characterized by rounded erythematous, dry, scaling patches. The lesions have a predilection for nails, scalp, genitalia, extensor surfaces, and the lumbosacral region. Accelerated epidermopoiesis is considered to be the fundamental pathologic feature in

psoriasis. [NIH]

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]

**Psychogenic:** Produced or caused by psychic or mental factors rather than organic factors. [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]

**Psychopathology:** The study of significant causes and processes in the development of mental illness. [NIH]

**Psychosis:** A mental disorder characterized by gross impairment in reality testing as evidenced by delusions, hallucinations, markedly incoherent speech, or disorganized and agitated behaviour without apparent awareness on the part of the patient of the incomprehensibility of his behaviour; the term is also used in a more general sense to refer to mental disorders in which mental functioning is sufficiently impaired as to interfere grossly with the patient's capacity to meet the ordinary demands of life. Historically, the term has been applied to many conditions, e.g. manic-depressive psychosis, that were first described in psychotic patients, although many patients with the disorder are not judged psychotic. [EU]

**Psychosomatic:** Pertaining to the mind-body relationship; having bodily symptoms of psychic, emotional, or mental origin; called also psychophysiologic. [EU]

**Psychotherapy:** A generic term for the treatment of mental illness or emotional disturbances primarily by verbal or nonverbal communication. [NIH]

Psychotomimetic: Psychosis miming. [NIH]

**Puberty:** The period during which the secondary sex characteristics begin to develop and the capability of sexual reproduction is attained. [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 Edema:** An accumulation of an excessive amount of watery fluid in the lungs, may be caused by acute exposure to dangerous concentrations of irritant gasses. [NIH]

Pulmonary hypertension: Abnormally high blood pressure in the arteries of the lungs. [NIH]

Pulsation: A throb or rhythmical beat, as of the heart. [EU]

Pulse: The rhythmical expansion and contraction of an artery produced by waves of

pressure caused by the ejection of blood from the left ventricle of the heart as it contracts. [NIH]

Pupil: The aperture in the iris through which light passes. [NIH]

**Purulent:** Consisting of or containing pus; associated with the formation of or caused by pus. [EU]

**Pustular:** Pertaining to or of the nature of a pustule; consisting of pustules (= a visible collection of pus within or beneath the epidermis). [EU]

Pyoderma: Any purulent skin disease (Dorland, 27th ed). [NIH]

**Pyoderma Gangrenosum:** An idiopathic, rapidly evolving, and severely debilitating disease occurring most commonly in association with chronic ulcerative colitis. It is characterized by the presence of boggy, purplish ulcers with undermined borders, appearing mostly on the legs. The majority of cases are in people between 40 and 60 years old. Its etiology is unknown. [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]

**Radial Artery:** The direct continuation of the brachial trunk, originating at the bifurcation of the brachial artery opposite the neck of the radius. Its branches may be divided into three groups corresponding to the three regions in which the vessel is situated, the forearm, wrist, and hand. [NIH]

**Radiation:** Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

**Radiation therapy:** The use of high-energy radiation from x-rays, gamma rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body in the area near cancer cells (internal radiation therapy, implant radiation, or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy. [NIH]

Radicular: Having the character of or relating to a radicle or root. [NIH]

**Radiculopathy:** Disease involving a spinal nerve root (see spinal nerve roots) which may result from compression related to intervertebral disk displacement; spinal cord injuries; spinal diseases; and other conditions. Clinical manifestations include radicular pain, weakness, and sensory loss referable to structures innervated by the involved nerve root. [NIH]

Radioactive: Giving off radiation. [NIH]

Radiofrequency ablation: The use of electrical current to destroy tissue. [NIH]

**Radioimmunotherapy:** Radiotherapy where cytotoxic radionuclides are linked to antibodies in order to deliver toxins directly to tumor targets. Therapy with targeted radiation rather than antibody-targeted toxins (immunotoxins) has the advantage that adjacent tumor cells, which lack the appropriate antigenic determinants, can be destroyed by radiation cross-fire. Radioimmunotherapy is sometimes called targeted radiotherapy, but this latter term can also refer to radionuclides linked to non-immune molecules (radiotherapy). [NIH] **Radiological:** Pertaining to radiodiagnostic and radiotherapeutic procedures, and interventional radiology or other planning and guiding medical radiology. [NIH]

**Radiotherapy:** The use of ionizing radiation to treat malignant neoplasms and other benign conditions. The most common forms of ionizing radiation used as therapy are x-rays, gamma rays, and electrons. A special form of radiotherapy, targeted radiotherapy, links a cytotoxic radionuclide to a molecule that targets the tumor. When this molecule is an antibody or other immunologic molecule, the technique is called radioimmunotherapy. [NIH]

**Radius:** The lateral bone of the forearm. [NIH]

**Random Allocation:** A process involving chance used in therapeutic trials or other research endeavor for allocating experimental subjects, human or animal, between treatment and control groups, or among treatment groups. It may also apply to experiments on inanimate objects. [NIH]

**Randomization:** Also called random allocation. Is allocation of individuals to groups, e.g., for experimental and control regimens, by chance. Within the limits of chance variation, random allocation should make the control and experimental groups similar at the start of an investigation and ensure that personal judgment and prejudices of the investigator do not influence allocation. [NIH]

**Randomized:** Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

**Randomized clinical trial:** A study in which the participants are assigned by chance to separate groups that compare different treatments; neither the researchers nor the participants can choose which group. Using chance to assign people to groups means that the groups will be similar and that the treatments they receive can be compared objectively. At the time of the trial, it is not known which treatment is best. It is the patient's choice to be in a randomized trial. [NIH]

**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]

Rape: Unlawful sexual intercourse without consent of the victim. [NIH]

**Reagent:** A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

**Reality Testing:** The individual's objective evaluation of the external world and the ability to differentiate adequately between it and the internal world; considered to be a primary ego function. [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]

**Receptors, Glutamate:** Cell-surface proteins that bind glutamate and trigger changes which influence the behavior of cells. Glutamate receptors include ionotropic receptors (AMPA, kainate, and N-methyl-D-aspartate receptors), which directly control ion channels, and metabotropic receptors which act through second messenger systems. Glutamate receptors are the most common mediators of fast excitatory synaptic transmission in the central nervous system. They have also been implicated in the mechanisms of memory and of many diseases. [NIH]

**Receptors, Serotonin:** Cell-surface proteins that bind serotonin and trigger intracellular changes which influence the behavior of cells. Several types of serotonin receptors have been recognized which differ in their pharmacology, molecular biology, and mode of action. [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]

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]

**Red Nucleus:** A pinkish-yellow portion of the midbrain situated in the rostral mesencephalic tegmentum. It receives a large projection from the contralateral half of the cerebellum via the superior cerebellar peduncle and a projection from the ipsilateral motor cortex. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

**Reflex:** An involuntary movement or exercise of function in a part, excited in response to a stimulus applied to the periphery and transmitted to the brain or spinal cord. [NIH]

Reflux: The term used when liquid backs up into the esophagus from the stomach. [NIH]

**Refraction:** A test to determine the best eyeglasses or contact lenses to correct a refractive error (myopia, hyperopia, or astigmatism). [NIH]

**Refractive Errors:** Deviations from the average or standard indices of refraction of the eye through its dioptric or refractive apparatus. [NIH]

**Refractive Power:** The ability of an object, such as the eye, to bend light as light passes through it. [NIH]

**Refractory:** Not readily yielding to treatment. [EU]

**Regimen:** A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

**Rehabilitative:** Instruction of incapacitated individuals or of those affected with some mental disorder, so that some or all of their lost ability may be regained. [NIH]

Relapse: The return of signs and symptoms of cancer after a period of improvement. [NIH]

**Reliability:** Used technically, in a statistical sense, of consistency of a test with itself, i. e. the extent to which we can assume that it will yield the same result if repeated a second time. [NIH]

**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]

**Renal cell cancer:** Cancer that develops in the lining of the renal tubules, which filter the blood and produce urine. [NIH]

**Renal pelvis:** The area at the center of the kidney. Urine collects here and is funneled into the ureter, the tube that connects the kidney to the bladder. [NIH]

**Renal tubular:** A defect in the kidneys that hinders their normal excretion of acids. Failure to excrete acids can lead to weak bones, kidney stones, and poor growth in children. [NIH]

**Renal tubular acidosis:** A rare disorder in which structures in the kidney that filter the blood are impaired, producing using that is more acid than normal. [NIH]

**Renin:** An enzyme which is secreted by the kidney and is formed from prorenin in plasma and kidney. The enzyme cleaves the Leu-Leu bond in angiotensinogen to generate angiotensin I. EC 3.4.23.15. (Formerly EC 3.4.99.19). [NIH]

**Reperfusion:** Restoration of blood supply to tissue which is ischemic due to decrease in normal blood supply. The decrease may result from any source including atherosclerotic obstruction, narrowing of the artery, or surgical clamping. It is primarily a procedure for treating infarction or other ischemia, by enabling viable ischemic tissue to recover, thus limiting further necrosis. However, it is thought that reperfusion can itself further damage the ischemic tissue, causing reperfusion injury. [NIH]

**Reperfusion Injury:** Functional, metabolic, or structural changes, including necrosis, in ischemic tissues thought to result from reperfusion to ischemic areas of the tissue. The most common instance is myocardial reperfusion injury. [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]

**Respiration:** The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

**Restoration:** Broad term applied to any inlay, crown, bridge or complete denture which restores or replaces loss of teeth or oral tissues. [NIH]

**Retina:** The ten-layered nervous tissue membrane of the eye. It is continuous with the optic nerve and receives images of external objects and transmits visual impulses to the brain. Its outer surface is in contact with the choroid and the inner surface with the vitreous body. The outer-most layer is pigmented, whereas the inner nine layers are transparent. [NIH]

**Retinal:** 1. Pertaining to the retina. 2. The aldehyde of retinol, derived by the oxidative enzymatic splitting of absorbed dietary carotene, and having vitamin A activity. In the retina, retinal combines with opsins to form visual pigments. One isomer, 11-cis retinal combines with opsin in the rods (scotopsin) to form rhodopsin, or visual purple. Another, all-trans retinal (trans-r.); visual yellow; xanthopsin) results from the bleaching of rhodopsin by light, in which the 11-cis form is converted to the all-trans form. Retinal also combines with opsins in the cones (photopsins) to form the three pigments responsible for colour vision. Called also retinal, and retinene1. [EU]

Retinal Hemorrhage: Bleeding from the vessels of the retina. [NIH]

**Retinitis:** Inflammation of the retina. It is rarely limited to the retina, but is commonly associated with diseases of the choroid (chorioretinitis) and of the optic nerve (neuroretinitis). The disease may be confined to one eye, but since it is generally dependent on a constitutional factor, it is almost always bilateral. It may be acute in course, but as a rule it lasts many weeks or even several months. [NIH]

**Retinoblastoma:** An eye cancer that most often occurs in children younger than 5 years. It occurs in hereditary and nonhereditary (sporadic) forms. [NIH]

**Retinoids:** Derivatives of vitamin A. Used clinically in the treatment of severe cystic acne, psoriasis, and other disorders of keratinization. Their possible use in the prophylaxis and treatment of cancer is being actively explored. [NIH]

**Retinol:** Vitamin A. It is essential for proper vision and healthy skin and mucous membranes. Retinol is being studied for cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Retinopathy: 1. Retinitis (= inflammation of the retina). 2. Retinosis (= degenerative,

noninflammatory condition of the retina). [EU]

**Retreatment:** The therapy of the same disease in a patient, with the same agent or procedure repeated after initial treatment, or with an additional or alternate measure or follow-up. It does not include therapy which requires more than one administration of a therapeutic agent or regimen. Retreatment is often used with reference to a different modality when the original one was inadequate, harmful, or unsuccessful. [NIH]

**Retrograde:** 1. Moving backward or against the usual direction of flow. 2. Degenerating, deteriorating, or catabolic. [EU]

**Retroperitoneal:** Having to do with the area outside or behind the peritoneum (the tissue that lines the abdominal wall and covers most of the organs in the abdomen). [NIH]

**Retrospective:** Looking back at events that have already taken place. [NIH]

**Rheumatic Diseases:** Disorders of connective tissue, especially the joints and related structures, characterized by inflammation, degeneration, or metabolic derangement. [NIH]

**Rheumatism:** A group of disorders marked by inflammation or pain in the connective tissue structures of the body. These structures include bone, cartilage, and fat. [NIH]

Rheumatoid: Resembling rheumatism. [EU]

**Rheumatoid arthritis:** A form of arthritis, the cause of which is unknown, although infection, hypersensitivity, hormone imbalance and psychologic stress have been suggested as possible causes. [NIH]

Rhinitis: Inflammation of the mucous membrane of the nose. [NIH]

Rhinorrhea: The free discharge of a thin nasal mucus. [EU]

**Riboflavin:** Nutritional factor found in milk, eggs, malted barley, liver, kidney, heart, and leafy vegetables. The richest natural source is yeast. It occurs in the free form only in the retina of the eye, in whey, and in urine; its principal forms in tissues and cells are as FMN and FAD. [NIH]

Ribose: A pentose active in biological systems usually in its D-form. [NIH]

Rigidity: Stiffness or inflexibility, chiefly that which is abnormal or morbid; rigor. [EU]

**Risk factor:** A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Rod: A reception for vision, located in the retina. [NIH]

**Rye:** A hardy grain crop, Secale cereale, grown in northern climates. It is the most frequent host to ergot (claviceps), the toxic fungus. Its hybrid with wheat is triticale, another grain. [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]

Salicylate: Non-steroidal anti-inflammatory drugs. [NIH]

Saline: A solution of salt and water. [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]

**Sarcoma:** A connective tissue neoplasm formed by proliferation of mesodermal cells; it is usually highly malignant. [NIH]

**Scans:** Pictures of structures inside the body. Scans often used in diagnosing, staging, and monitoring disease include liver scans, bone scans, and computed tomography (CT) or computerized axial tomography (CAT) scans and magnetic resonance imaging (MRI) scans. In liver scanning and bone scanning, radioactive substances that are injected into the bloodstream collect in these organs. A scanner that detects the radiation is used to create pictures. In CT scanning, an x-ray machine linked to a computer is used to produce detailed pictures of organs inside the body. MRI scans use a large magnet connected to a computer to create pictures of areas inside the body. [NIH]

**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]

**Schwannoma:** A tumor of the peripheral nervous system that begins in the nerve sheath (protective covering). It is almost always benign, but rare malignant schwannomas have been reported. [NIH]

**Sciatica:** A condition characterized by pain radiating from the back into the buttock and posterior/lateral aspects of the leg. Sciatica may be a manifestation of sciatic neuropathy; radiculopathy (involving the L4, L5, S1 or S2 spinal nerve roots; often associated with intervertebral disk displacement); or lesions of the cauda equina. [NIH]

**Scleroderma:** A chronic disorder marked by hardening and thickening of the skin. Scleroderma can be localized or it can affect the entire body (systemic). [NIH]

**Sclerosis:** A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Scoliosis: A lateral curvature of the spine. [NIH]

**Scotoma:** A localized defect in the visual field bordered by an area of normal vision. This occurs with a variety of eye diseases (e.g., retinal diseases and glaucoma), optic nerve diseases, and other conditions. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Sebaceous: Gland that secretes sebum. [NIH]

Sebaceous gland: Gland that secretes sebum. [NIH]

**Second Messenger Systems:** Systems in which an intracellular signal is generated in response to an intercellular primary messenger such as a hormone or neurotransmitter. They are intermediate signals in cellular processes such as metabolism, secretion, contraction, phototransduction, and cell growth. Examples of second messenger systems are the adenyl cyclase-cyclic AMP system, the phosphatidylinositol diphosphate-inositol triphosphate system, and the cyclic GMP system. [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]

**Secretory Vesicles:** Vesicles derived from the golgi apparatus containing material to be released at the cell surface. [NIH]

Sedative: 1. Allaying activity and excitement. 2. An agent that allays excitement. [EU]

**Sedatives, Barbiturate:** Those derivatives of barbituric or thiobarbituric acid that are used as hypnotics or sedatives. The structural class of all such derivatives, regardless of use, is barbiturates. [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 Care:** Performance of activities or tasks traditionally performed by professional health care providers. The concept includes care of oneself or one's family and friends. [NIH]

**Sella:** A deep depression in the shape of a Turkish saddle in the upper surface of the body of the sphenoid bone in the deepest part of which is lodged the hypophysis cerebri. [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]

Semisynthetic: Produced by chemical manipulation of naturally occurring substances. [EU]

**Senile:** Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

**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]

**Sensitization:** 1. Administration of antigen to induce a primary immune response; priming; immunization. 2. Exposure to allergen that results in the development of hypersensitivity. 3. The coating of erythrocytes with antibody so that they are subject to lysis by complement in the presence of homologous antigen, the first stage of a complement fixation test. [EU]

**Sensory loss:** A disease of the nerves whereby the myelin or insulating sheath of myelin on the nerves does not stay intact and the messages from the brain to the muscles through the nerves are not carried properly. [NIH]

Septic: Produced by or due to decomposition by microorganisms; putrefactive. [EU]

**Serotonin:** A biochemical messenger and regulator, synthesized from the essential amino acid L-tryptophan. In humans it is found primarily in the central nervous system, gastrointestinal tract, and blood platelets. Serotonin mediates several important physiological functions including neurotransmission, gastrointestinal motility, hemostasis, and cardiovascular integrity. Multiple receptor families (receptors, serotonin) explain the broad physiological actions and distribution of this biochemical mediator. [NIH]

**Serotonin Agonists:** Agents that have an affinity for serotonin receptors and are able to mimic the effects of serotonin by stimulating the physiologic activity at the cell receptors. These compounds are used as antidepressants, anxiolytics, and in the treatment of migraine. [NIH]

Serotonin Antagonists: Drugs that bind to but do not activate serotonin receptors, thereby
blocking the actions of serotonin or serotonin agonists. [NIH]

**Serotonin Uptake Inhibitors:** Compounds that specifically inhibit the reuptake of serotonin in the brain. This increases the serotonin concentration in the synaptic cleft which then activates serotonin receptors to a greater extent. These agents have been used in treatment of depression, panic disorder, obsessive-compulsive behavior, and alcoholism, as analgesics, and to treat obesity and bulimia. Many of the adrenergic uptake inhibitors also inhibit serotonin uptake; they are not included here. [NIH]

Serous: Having to do with serum, the clear liquid part of blood. [NIH]

**Serum:** The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

**Sex Characteristics:** Those characteristics that distinguish one sex from the other. The primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

**Sex Determination:** The biological characteristics which distinguish human beings as female or male. [NIH]

**Shock:** The general bodily disturbance following a severe injury; an emotional or moral upset occasioned by some disturbing or unexpected experience; disruption of the circulation, which can upset all body functions: sometimes referred to as circulatory shock. [NIH]

**Shoulder Pain:** Unilateral or bilateral pain of the shoulder. It is often caused by physical activities such as work or sports participation, but may also be pathologic in origin. [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 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]

**Signs and Symptoms:** Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [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]

**Sleep Bruxism:** A sleep disorder characterized by grinding and clenching of the teeth and forceful lateral or protrusive jaw movements. Sleep bruxism may be associated with tooth injuries; temporomandibular joint disorders; sleep disturbances; and other conditions. [NIH]

**Small intestine:** The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

**Smooth muscle:** Muscle that performs automatic tasks, such as constricting blood vessels. [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 Support:** Support systems that provide assistance and encouragement to individuals with physical or emotional disabilities in order that they may better cope. Informal social support is usually provided by friends, relatives, or peers, while formal assistance is provided by churches, groups, etc. [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]

**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]

**Somatostatin:** A polypeptide hormone produced in the hypothalamus, and other tissues and organs. It inhibits the release of human growth hormone, and also modulates important physiological functions of the kidney, pancreas, and gastrointestinal tract. Somatostatin receptors are widely expressed throughout the body. Somatostatin also acts as a neurotransmitter in the central and peripheral nervous systems. [NIH]

Somnolence: Sleepiness; also unnatural drowsiness. [EU]

**Spasm:** An involuntary contraction of a muscle or group of muscles. Spasms may involve skeletal muscle or smooth muscle. [NIH]

**Spasmodic:** Of the nature of a spasm. [EU]

**Spastic:** 1. Of the nature of or characterized by spasms. 2. Hypertonic, so that the muscles are stiff and the movements awkward. 3. A person exhibiting spasticity, such as occurs in spastic paralysis or in cerebral palsy. [EU]

**Spasticity:** A state of hypertonicity, or increase over the normal tone of a muscle, with heightened deep tendon reflexes. [EU]

**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]

**Sperm:** The fecundating fluid of the male. [NIH]

**Sphenoid:** An unpaired cranial bone with a body containing the sphenoid sinus and forming the posterior part of the medial walls of the orbits. [NIH]

**Sphincter:** A ringlike band of muscle fibres that constricts a passage or closes a natural orifice; called also musculus sphincter. [EU]

**Spices:** The dried seeds, bark, root, stems, buds, leaves, or fruit of aromatic plants used to season food. [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]

**Spinal Cord Diseases:** Pathologic conditions which feature spinal cord damage or dysfunction, including disorders involving the meninges and perimeningeal spaces surrounding the spinal cord. Traumatic injuries, vascular diseases, infections, and inflammatory/autoimmune processes may affect the spinal cord. [NIH]

**Spinal Cord Injuries:** Penetrating and non-penetrating injuries to the spinal cord resulting from traumatic external forces (e.g., wounds, gunshot; whiplash injuries; etc.). [NIH]

**Spinal Nerve Roots:** The paired bundles of nerve fibers entering and leaving the spinal cord at each segment. The dorsal and ventral nerve roots join to form the mixed segmental spinal nerves. The dorsal roots are generally afferent, formed by the central projections of the spinal (dorsal root) ganglia sensory cells, and the ventral roots efferent, comprising the axons of spinal motor and autonomic preganglionic neurons. There are, however, some exceptions to this afferent/efferent rule. [NIH]

**Spinal tap:** A procedure in which a needle is put into the lower part of the spinal column to collect cerebrospinal fluid or to give anticancer drugs intrathecally. Also called a lumbar puncture. [NIH]

**Spiramycin:** A macrolide antibiotic produced by Streptomyces ambofaciens. The drug is effective against gram-positive aerobic pathogens, N. gonorrhoeae, and staphylococci. It is used to treat infections caused by bacteria and Toxoplasma gondii. [NIH]

Spirochete: Lyme disease. [NIH]

Spleen: An organ that is part of the lymphatic system. The spleen produces lymphocytes,

filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach. [NIH]

Spondylitis: Inflammation of the vertebrae. [EU]

Spondylolisthesis: Forward displacement of one vertebra over another. [NIH]

**Sporadic:** Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

**Spores:** The reproductive elements of lower organisms, such as protozoa, fungi, and cryptogamic plants. [NIH]

**Sprains and Strains:** A collective term for muscle and ligament injuries without dislocation or fracture. A sprain is a joint injury in which some of the fibers of a supporting ligament are ruptured but the continuity of the ligament remains intact. A strain is an overstretching or overexertion of some part of the musculature. [NIH]

Sprue: A non febrile tropical disease of uncertain origin. [NIH]

Stabilization: The creation of a stable state. [EU]

**Staging:** Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

**Standard therapy:** A currently accepted and widely used treatment for a certain type of cancer, based on the results of past research. [NIH]

Standardize: To compare with or conform to a standard; to establish standards. [EU]

**Stasis:** A word termination indicating the maintenance of (or maintaining) a constant level; preventing increase or multiplication. [EU]

**Status Epilepticus:** Repeated and prolonged epileptic seizures without recovery of consciousness between attacks. [NIH]

**Steel:** A tough, malleable, iron-based alloy containing up to, but no more than, two percent carbon and often other metals. It is used in medicine and dentistry in implants and instrumentation. [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]

**Stimulant:** 1. Producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. An agent or remedy that produces stimulation. [EU]

**Stimulus:** That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

**Stomach:** An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Stool: The waste matter discharged in a bowel movement; feces. [NIH]

**Strabismus:** Deviation of the eye which the patient cannot overcome. The visual axes assume a position relative to each other different from that required by the physiological

conditions. The various forms of strabismus are spoken of as tropias, their direction being indicated by the appropriate prefix, as cyclo tropia, esotropia, exotropia, hypertropia, and hypotropia. Called also cast, heterotropia, manifest deviation, and squint. [EU]

Strained: A stretched condition of a ligament. [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]

**Stress management:** A set of techniques used to help an individual cope more effectively with difficult situations in order to feel better emotionally, improve behavioral skills, and often to enhance feelings of control. Stress management may include relaxation exercises, assertiveness training, cognitive restructuring, time management, and social support. It can be delivered either on a one-to-one basis or in a group format. [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]

**Strychnine:** An alkaloid found in the seeds of nux vomica. It is a competitive antagonist at glycine receptors and thus a convulsant. It has been used as an analeptic, in the treatment of nonketotic hyperglycinemia and sleep apnea, and as a rat poison. [NIH]

**Stupor:** Partial or nearly complete unconsciousness, manifested by the subject's responding only to vigorous stimulation. Also, in psychiatry, a disorder marked by reduced responsiveness. [EU]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subarachnoid: Situated or occurring between the arachnoid and the pia mater. [EU]

**Subclavian:** The direct continuation of the axillary vein at the lateral border of the first rib. It passes medially to join the internal jugular vein and form the brachiocephalic vein on each side. [NIH]

**Subclavian Artery:** Artery arising from the brachiocephalic trunk on the right side and from the arch of the aorta on the left side. It distributes to the neck, thoracic wall, spinal cord, brain, meninges, and upper limb. [NIH]

**Subclavian Vein:** The continuation of the axillary vein which follows the subclavian artery and then joins the internal jugular vein to form the brachiocephalic vein. [NIH]

**Subclinical:** Without clinical manifestations; said of the early stage(s) of an infection or other disease or abnormality before symptoms and signs become apparent or detectable by clinical examination or laboratory tests, or of a very mild form of an infection or other disease or abnormality. [EU]

Subcutaneous: Beneath the skin. [NIH]

**Subspecies:** A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

**Substance P:** An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

**Sulfadiazine:** A short-acting sulfonamide used in combination with pyrimethamine to treat toxoplasmosis in patients with acquired immunodeficiency syndrome and in newborns with congenital infections. [NIH]

Sulfur: An element that is a member of the chalcogen family. It has an atomic symbol S,

atomic number 16, and atomic weight 32.066. It is found in the amino acids cysteine and methionine. [NIH]

**Sumatriptan:** A serotonin agonist that acts selectively at 5HT1 receptors. It is used in the treatment of migraines. [NIH]

**Support group:** A group of people with similar disease who meet to discuss how better to cope with their cancer and treatment. [NIH]

**Supportive care:** Treatment given to prevent, control, or relieve complications and side effects and to improve the comfort and quality of life of people who have cancer. [NIH]

**Suppression:** A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

**Supraorbital:** The branch of the frontal nerve that passes through the supraorbital notch or foramen and is sensory for the upper eyelid, the conjunctiva, the eyebrow, the forehead, and the scalp up to the occipital bone. [NIH]

**Sympathectomy:** The removal or interruption of some part of the sympathetic nervous system for therapeutic or research purposes. [NIH]

**Sympathetic Nervous System:** The thoracolumbar division of the autonomic nervous system. Sympathetic preganglionic fibers originate in neurons of the intermediolateral column of the spinal cord and project to the paravertebral and prevertebral ganglia, which in turn project to target organs. The sympathetic nervous system mediates the body's response to stressful situations, i.e., the fight or flight reactions. It often acts reciprocally to the parasympathetic system. [NIH]

**Sympathomimetic:** 1. Mimicking the effects of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. 2. An agent that produces effects similar to those of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. Called also adrenergic. [EU]

Symphysis: A secondary cartilaginous joint. [NIH]

Symptomatic: Having to do with symptoms, which are signs of a condition or disease. [NIH]

**Symptomatology:** 1. That branch of medicine with treats of symptoms; the systematic discussion of symptoms. 2. The combined symptoms of a disease. [EU]

**Synapses:** Specialized junctions at which a neuron communicates with a target cell. At classical synapses, a neuron's presynaptic terminal releases a chemical transmitter stored in synaptic vesicles which diffuses across a narrow synaptic cleft and activates receptors on the postsynaptic membrane of the target cell. The target may be a dendrite, cell body, or axon of another neuron, or a specialized region of a muscle or secretory cell. Neurons may also communicate through direct electrical connections which are sometimes called electrical synapses; these are not included here but rather in gap junctions. [NIH]

**Synapsis:** The pairing between homologous chromosomes of maternal and paternal origin during the prophase of meiosis, leading to the formation of gametes. [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]

**Synaptic Transmission:** The communication from a neuron to a target (neuron, muscle, or secretory cell) across a synapse. In chemical synaptic transmission, the presynaptic neuron releases a neurotransmitter that diffuses across the synaptic cleft and binds to specific synaptic receptors. These activated receptors modulate ion channels and/or second-

messenger systems to influence the postsynaptic cell. Electrical transmission is less common in the nervous system, and, as in other tissues, is mediated by gap junctions. [NIH]

**Synaptic Vesicles:** Membrane-bound compartments which contain transmitter molecules. Synaptic vesicles are concentrated at presynaptic terminals. They actively sequester transmitter molecules from the cytoplasm. In at least some synapses, transmitter release occurs by fusion of these vesicles with the presynaptic membrane, followed by exocytosis of their contents. [NIH]

**Syncope:** A temporary suspension of consciousness due to generalized cerebral schemia, a faint or swoon. [EU]

**Syncytium:** A living nucleated tissue without apparent cellular structure; a tissue composed of a mass of nucleated protoplasm without cell boundaries. [NIH]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Synovial: Of pertaining to, or secreting synovia. [EU]

Systemic: Affecting the entire body. [NIH]

**Systemic lupus erythematosus:** SLE. A chronic inflammatory connective tissue disease marked by skin rashes, joint pain and swelling, inflammation of the kidneys, inflammation of the fibrous tissue surrounding the heart (i.e., the pericardium), as well as other problems. Not all affected individuals display all of these problems. May be referred to as lupus. [NIH]

**Systolic:** Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

**Tachycardia:** Excessive rapidity in the action of the heart, usually with a heart rate above 100 beats per minute. [NIH]

**Tacrolimus:** A macrolide isolated from the culture broth of a strain of Streptomyces tsukubaensis that has strong immunosuppressive activity in vivo and prevents the activation of T-lymphocytes in response to antigenic or mitogenic stimulation in vitro. [NIH]

**Tardive:** Marked by lateness, late; said of a disease in which the characteristic lesion is late in appearing. [EU]

**Tear Gases:** Gases that irritate the eyes, throat, or skin. Severe lacrimation develops upon irritation of the eyes. [NIH]

**Telangiectasia:** The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

**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]

Temporal Lobe: Lower lateral part of the cerebral hemisphere. [NIH]

**Tennis Elbow:** A condition characterized by pain in or near the lateral humeral epicondyle or in the forearm extensor muscle mass as a result of unusual strain. It occurs in tennis players as well as housewives, artisans, and violinists. [NIH]

Terminalis: A groove on the lateral surface of the right atrium. [NIH]

**Tetracycline:** An antibiotic originally produced by Streptomyces viridifaciens, but used mostly in synthetic form. It is an inhibitor of aminoacyl-tRNA binding during protein synthesis. [NIH]

Thalamic: Cell that reaches the lateral nucleus of amygdala. [NIH]

**Thalamic Diseases:** Disorders of the centrally located thalamus, which integrates a wide range of cortical and subcortical information. Manifestations include sensory loss, movement disorders; ataxia, pain syndromes, visual disorders, a variety of

neuropsychological conditions, and coma. Relatively common etiologies include cerebrovascular disorders; craniocerebral trauma; brain neoplasms; brain hypoxia; intracranial hemorrhages; and infectious processes. [NIH]

**Thalamus:** Paired bodies containing mostly gray substance and forming part of the lateral wall of the third ventricle of the brain. The thalamus represents the major portion of the diencephalon and is commonly divided into cellular aggregates known as nuclear groups. [NIH]

**Therapeutics:** The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thermal: Pertaining to or characterized by heat. [EU]

**Third Ventricle:** A narrow cleft inferior to the corpus callosum, within the diencephalon, between the paired thalami. Its floor is formed by the hypothalamus, its anterior wall by the lamina terminalis, and its roof by ependyma. It communicates with the fourth ventricle by the cerebral aqueduct, and with the lateral ventricles by the interventricular foramina. [NIH]

Thoracic: Having to do with the chest. [NIH]

Thoracic Outlet Syndrome: A neurovascular syndrome associated with compression of the brachial plexus; subclavian artery; and subclavian vein at the superior thoracic outlet. This may result from a variety of anomalies such as a cervical rib (cervical rib syndrome), anomalous fascial bands, and abnormalities of the origin or insertion of the anterior or medial scalene muscles. Clinical features may include pain in the shoulder and neck region which radiates into the arm, paresis or paralysis of brachial plexus innervated muscles, paresthesia, loss of sensation, reduction of arterial pulses in the affected extremity, ischemia, and edema. (Adams et al., Principles of Neurology, 6th ed, pp214-5). [NIH]

Thorax: A part of the trunk between the neck and the abdomen; the chest. [NIH]

**Threshold:** For a specified sensory modality (e. g. light, sound, vibration), the lowest level (absolute threshold) or smallest difference (difference threshold, difference limen) or intensity of the stimulus discernible in prescribed conditions of stimulation. [NIH]

**Thrombin:** An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

**Thrombocytes:** Blood cells that help prevent bleeding by causing blood clots to form. Also called platelets. [NIH]

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]

Thrombophlebitis: Inflammation of a vein associated with thrombus formation. [NIH]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

**Thrombus:** An aggregation of blood factors, primarily platelets and fibrin with entrapment of cellular elements, frequently causing vascular obstruction at the point of its formation. Some authorities thus differentiate thrombus formation from simple coagulation or clot formation. [EU]

**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]

Time Management: Planning and control of time to improve efficiency and effectiveness.

[NIH]

**Tin:** A trace element that is required in bone formation. It has the atomic symbol Sn, atomic number 50, and atomic weight 118.71. [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]

**Tolerance:** 1. The ability to endure unusually large doses of a drug or toxin. 2. Acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

**Tomography:** Imaging methods that result in sharp images of objects located on a chosen plane and blurred images located above or below the plane. [NIH]

**Tonic:** 1. Producing and restoring the normal tone. 2. Characterized by continuous tension. 3. A term formerly used for a class of medicinal preparations believed to have the power of restoring normal tone to tissue. [EU]

**Tonicity:** The normal state of muscular tension. [NIH]

**Tooth Injuries:** Traumatic or other damage to teeth including fractures (tooth fractures) or displacements (tooth luxation). [NIH]

**Tooth Movement:** Orthodontic techniques used to correct the malposition of a single tooth. [NIH]

**Tooth Preparation:** Procedures carried out with regard to the teeth or tooth structures preparatory to specified dental therapeutic and surgical measures. [NIH]

Toothache: Pain in the adjacent areas of the teeth. [NIH]

**Topical:** On the surface of the body. [NIH]

**Torticollis:** Wryneck; a contracted state of the cervical muscles, producing twisting of the neck and an unnatural position of the head. [EU]

**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]

**Toxins:** Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals. [NIH]

**Toxoplasmosis:** The acquired form of infection by Toxoplasma gondii in animals and man. [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]

Tramadol: A narcotic analgesic proposed for severe pain. It may be habituating. [NIH]

Transcutaneous: Transdermal. [EU]

**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]

**Translational:** The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

**Transmitter:** A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [NIH]

**Trauma:** Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [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]

**Trees:** Woody, usually tall, perennial higher plants (Angiosperms, Gymnosperms, and some Pterophyta) having usually a main stem and numerous branches. [NIH]

**Tricuspid Atresia:** Absence of the orifice between the right atrium and ventricle, with the presence of an atrial defect through which all the systemic venous return reaches the left heart. As a result, there is left ventricular hypertrophy because the right ventricle is absent or not functional. [NIH]

Tricyclic: Containing three fused rings or closed chains in the molecular structure. [EU]

**Trigeminal:** Cranial nerve V. It is sensory for the eyeball, the conjunctiva, the eyebrow, the skin of face and scalp, the teeth, the mucous membranes in the mouth and nose, and is motor to the muscles of mastication. [NIH]

**Trigeminal Ganglion:** The semilunar-shaped ganglion containing the cells of origin of most of the sensory fibers of the trigeminal nerve. It is situated within the dural cleft on the cerebral surface of the petrous portion of the temporal bone and gives off the ophthalmic, maxillary, and part of the mandibular nerves. [NIH]

**Trigeminal Nerve:** The 5th and largest cranial nerve. The trigeminal nerve is a mixed motor and sensory nerve. The larger sensory part forms the ophthalmic, mandibular, and maxillary nerves which carry afferents sensitive to external or internal stimuli from the skin, muscles, and joints of the face and mouth and from the teeth. Most of these fibers originate from cells of the trigeminal ganglion and project to the trigeminal nucleus of the brain stem. The smaller motor part arises from the brain stem trigeminal motor nucleus and innervates the muscles of mastication. [NIH]

**Trochlear Nerve:** The 4th cranial nerve. The trochlear nerve carries the motor innervation of the superior oblique muscles of the eye. [NIH]

**Trochlear Nerve Diseases:** Diseases of the fourth cranial (trochlear) nerve or its nucleus in the midbrain. The nerve crosses as it exits the midbrain dorsally and may be injured along its course through the intracranial space, cavernous sinus, superior orbital fissure, or orbit. Clinical manifestations include weakness of the superior oblique muscle which causes

vertical diplopia that is maximal when the affected eye is adducted and directed inferiorly. Head tilt may be seen as a compensatory mechanism for diplopia and rotation of the visual axis. Common etiologies include craniocerebral trauma and infratentorial neoplasms. [NIH]

**Tryptophan:** An essential amino acid that is necessary for normal growth in infants and for nitrogen balance in adults. It is a precursor serotonin and niacin. [NIH]

**Tuberculosis:** Any of the infectious diseases of man and other animals caused by species of Mycobacterium. [NIH]

**Tuberous Sclerosis:** A rare congenital disease in which the essential pathology is the appearance of multiple tumors in the cerebrum and in other organs, such as the heart or kidneys. [NIH]

**Tumor marker:** A substance sometimes found in an increased amount in the blood, other body fluids, or tissues and which may mean that a certain type of cancer is in the body. Examples of tumor markers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (prostate cancer). Also called biomarker. [NIH]

**Tumor Necrosis Factor:** Serum glycoprotein produced by activated macrophages and other mammalian mononuclear leukocytes which has necrotizing activity against tumor cell lines and increases ability to reject tumor transplants. It mimics the action of endotoxin but differs from it. It has a molecular weight of less than 70,000 kDa. [NIH]

**Tumour:** 1. Swelling, one of the cardinal signs of inflammations; morbid enlargement. 2. A new growth of tissue in which the multiplication of cells is uncontrolled and progressive; called also neoplasm. [EU]

**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]

Ulcer: A localized necrotic lesion of the skin or a mucous surface. [NIH]

Ulceration: 1. The formation or development of an ulcer. 2. An ulcer. [EU]

**Ulcerative colitis:** Chronic inflammation of the colon that produces ulcers in its lining. This condition is marked by abdominal pain, cramps, and loose discharges of pus, blood, and mucus from the bowel. [NIH]

**Unconscious:** Experience which was once conscious, but was subsequently rejected, as the "personal unconscious". [NIH]

**Uraemia:** 1. An excess in the blood of urea, creatinine, and other nitrogenous end products of protein and amino acids metabolism; more correctly referred to as azotemia. 2. In current usage the entire constellation of signs and symptoms of chronic renal failure, including nausea, vomiting anorexia, a metallic taste in the mouth, a uraemic odour of the breath, pruritus, uraemic frost on the skin, neuromuscular disorders, pain and twitching in the muscles, hypertension, edema, mental confusion, and acid-base and electrolyte imbalances. [EU]

Ureters: Tubes that carry urine from the kidneys to the bladder. [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]

**Urine:** Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Urogenital: Pertaining to the urinary and genital apparatus; genitourinary. [EU]

**Urticaria:** A vascular reaction of the skin characterized by erythema and wheal formation due to localized increase of vascular permeability. The causative mechanism may be allergy, infection, or stress. [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]

**Vaccine:** A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. [NIH]

**Vagina:** The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

Vaginal: Of or having to do with the vagina, the birth canal. [NIH]

Vaginitis: Inflammation of the vagina characterized by pain and a purulent discharge. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

**Vascular Headaches:** A group of disorders characterized by recurrent headaches associated with abnormal dilation and constriction of cerebral blood vessels. Representative disorders from this category include migraine, cluster headache, and paroxysmal hemicrania. [NIH]

**Vascular Resistance:** An expression of the resistance offered by the systemic arterioles, and to a lesser extent by the capillaries, to the flow of blood. [NIH]

Vasculitis: Inflammation of a blood vessel. [NIH]

**Vasoconstriction:** Narrowing of the blood vessels without anatomic change, for which constriction, pathologic is used. [NIH]

**Vasodilation:** Physiological dilation of the blood vessels without anatomic change. For dilation with anatomic change, dilatation, pathologic or aneurysm (or specific aneurysm) is used. [NIH]

Vasodilator: An agent that widens blood vessels. [NIH]

**Vasomotor:** 1. Affecting the calibre of a vessel, especially of a blood vessel. 2. Any element or agent that effects the calibre of a blood vessel. [EU]

VE: The total volume of gas either inspired or expired in one minute. [NIH]

**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]

**Venlafaxine:** An antidepressant drug that is being evaluated for the treatment of hot flashes in women who have breast cancer. [NIH]

**Venous:** Of or pertaining to the veins. [EU]

**Venous blood:** Blood that has given up its oxygen to the tissues and carries carbon dioxide back for gas exchange. [NIH]

**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]

**Vertebral Artery:** The first branch of the subclavian artery with distribution to muscles of the neck, vertebrae, spinal cord, cerebellum and interior of the cerebrum. [NIH]

**Vertebral Artery Dissection:** Dissection of the wall of the vertebral artery, leading to the formation of an aneurysm that may occlude the vessel. Thrombus formation may occur and give rise to emboli. Cervical fractures or related neck injuries and craniocerebral trauma are commonly associated conditions, although this process may occur spontaneously. Ischemia, infarction, and hemorrhage in the vascular distribution of the affected vertebral artery may complicate this condition. [NIH]

**Vertebrobasilar Insufficiency:** Localized or diffuse reduction in blood flow through the vertebrobasilar arterial system, which supplies the brain stem; cerebellum; occipital lobe; medial temporal lobe; and thalamus. Characteristic clinical features include syncope; lightheadedness; visual disturbances; and vertigo. brain stem infarctions or other brain infarction may be associated. [NIH]

**Vertigo:** An illusion of movement; a sensation as if the external world were revolving around the patient (objective vertigo) or as if he himself were revolving in space (subjective vertigo). The term is sometimes erroneously used to mean any form of dizziness. [EU]

**Vesicular:** 1. Composed of or relating to small, saclike bodies. 2. Pertaining to or made up of vesicles on the skin. [EU]

**Vestibular:** Pertaining to or toward a vestibule. In dental anatomy, used to refer to the tooth surface directed toward the vestibule of the mouth. [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]

**Vibrio:** A genus of Vibrionaceae, made up of short, slightly curved, motile, gram-negative rods. Various species produce cholera and other gastrointestinal disorders as well as abortion in sheep and cattle. [NIH]

Vibrio cholerae: The etiologic agent of cholera. [NIH]

**Villi:** The tiny, fingerlike projections on the surface of the small intestine. Villi help absorb nutrients. [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]

**Virulent:** A virus or bacteriophage capable only of lytic growth, as opposed to temperate phages establishing the lysogenic response. [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]

Visceral: , from viscus a viscus) pertaining to a viscus. [EU]

Visual Cortex: Area of the occipital lobe concerned with vision. [NIH]

**Visual field:** The entire area that can be seen when the eye is forward, including peripheral vision. [NIH]

**Visual Perception:** The selecting and organizing of visual stimuli based on the individual's past experience. [NIH]

**Vitamin A:** A substance used in cancer prevention; it belongs to the family of drugs called retinoids. [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]

Vitreous Hemorrhage: Hemorrhage into the vitreous body. [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]

Volition: Voluntary activity without external compulsion. [NIH]

**Vomica:** The profuse and sudden expectoration of pus and putrescent matter. An abnormal cavity in an organ especially in the lung, caused by suppuration and the breaking down of tissue. [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]

War: Hostile conflict between organized groups of people. [NIH]

**Weight-Bearing:** The physical state of supporting an applied load. This often refers to the weight-bearing bones or joints that support the body's weight, especially those in the spine, hip, knee, and foot. [NIH]

Wheezing: Breathing with a rasp or whistling sound; a sign of airway constriction or obstruction. [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]

**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]

**Yawning:** An involuntary deep inspiration with the mouth open, often accompanied by the act of stretching. [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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