DIARRHEA

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

JAMES N. PARKER, M.D.
AND PHILIP M. PARKER, PH.D., EDITORS

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About the Editors

James N. Parker, M.D.

Dr. James N. Parker received his Bachelor of Science degree in Psychobiology from the University of California, Riverside and his M.D. from the University of California, San Diego. In addition to authoring numerous research publications, he has lectured at various academic institutions. Dr. Parker is the medical editor for health books by ICON Health Publications.

Philip M. Parker, Ph.D.

Philip M. Parker is the Eli Lilly Chair Professor of Innovation, Business and Society at INSEAD (Fontainebleau, France and Singapore). Dr. Parker has also been Professor at the University of California, San Diego and has taught courses at Harvard University, the Hong Kong University of Science and Technology, the Massachusetts Institute of Technology, Stanford University, and UCLA. Dr. Parker is the associate editor for ICON Health Publications.

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ICON Group International, Inc.
4370 La Jolla Village Drive, Fourth Floor
San Diego, CA 92122 USA
Fax: 858-546-4341
Web site: **www.icongrouponline.com/health**

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FORWARD

In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[1] Furthermore, because of the rapid increase in Internet-based information, many hours can be wasted searching, selecting, and printing. Since only the smallest fraction of information dealing with diarrhea 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 diarrhea, 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 diarrhea, 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 diarrhea. 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 diarrhea, 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 diarrhea.

The Editors

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

CHAPTER 1. STUDIES ON DIARRHEA

Overview

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

The Combined Health Information Database

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

- **Diarrhea-Constipation-Pain: When is It Irritable Bowel Syndrome?**

  Source: Consultant. 41(8): 1089-1091, 1095-1096. July 2001.

  Contact: Available from Cliggott Publishing Company. 55 Holly Hill Lane, Box 4010, Greenwich, CT 06831-0010.

  Summary: Central to the diagnosis of irritable bowel syndrome (IBS) are the symptoms of abdominal pain and disordered defecation of at least 3 months' duration. This article helps physicians determine when the symptoms of diarrhea, or constipation, or pain are indeed due to IBS. Either diarrhea or constipation can predominate, although the defecation pattern may vary from day to day in some patients. In the absence of evidence of more serious disease, diagnosis is based largely on the results of a thorough history and examination. For most patients, general screening tests include a complete

blood cell count, erythrocyte sedimentation rate, serum chemistry panel, stool guaiac test, and stool examination for ova (eggs) and parasites. For patients older than 50 years, flexible sigmoidoscopy, colonoscopy, or barium enema may be indicated. Management of IBS consists of patient education and reassurance; dietary modification, including increased fiber intake in patients with constipation; and in some cases, judicious use of medications or psychological interventions. 2 tables. 35 references.

- **Investigation of Diarrhea in AIDS**

  Source: Canadian Journal of Gastroenterology. 14(11): 933-940. December 2000.

  Contact: Available from Pulsus Group, Inc. 2902 South Sheridan Way, Oakville, Ontario, Canada L6J 7L6. Fax (905) 829-4799. E-mail: pulsus@pulsus.com.

  Summary: Chronic diarrhea is a common problem in patients with AIDS, resulting in significant morbidity (illness) and potential mortality (death). In the early stages of immunodeficiency, HIV infected patients are susceptible to infection with the same enteric pathogens that cause diarrhea in immunocompetent hosts, but with progressive immunodeficiency, these patients become susceptible to numerous opportunistic disorders. This article reviews the investigation of diarrhea in patients with AIDS. The main factor to consider when tailoring the work up of diarrhea in the HIV infected patient is the immune status, which is reflected by the total CD4 lymphocyte cell count. A CD4 count of less than 100 cells per microliter is significantly correlated with opportunistic disorders. For the HIV infected patient with diarrhea, repeated stool studies to investigate for bacteria, ova (eggs of parasites), and parasites should be the first step. When either upper or lower gastrointestinal tract symptoms are present and stool studies are negative, endoscopy directed to the probable organ of involvement is appropriate. If localizing symptoms are absent, the most appropriate next test is sigmoidoscopy with biopsies. Not infrequently, despite extensive evaluation, the cause of diarrhea in patients with AIDS remains unexplained. Recently, the widespread use of highly active antiretroviral therapy, including protease inhibitors, has led to a change in the epidemiology of diarrhea in AIDS patients. As their immune status improves, HIV infected patients treated with combination therapy become less prone to opportunistic disorders. However, diarrhea appears to be frequent because several antiretroviral agents can themselves cause diarrhea. 3 tables. 58 references.

- **Bile Acid Malabsorption as a Cause of Chronic Diarrhea**

  Source: Digestive Diseases and Sciences. 44(1): 14-19. January 1999.

  Summary: Chronic diarrhea may be caused by a broad spectrum of disease processes, which are usually identified by a combination of patient history, clinical examination, analysis of stool specimens, and endoscopic procedures. In some patients, however, the routine workup fails to yield a clear diagnosis. In this latter group with chronic diarrhea of unknown origin, bile acid malabsorption is thought to play a causative role in up to one third of patients. This article reports on a study undertaken to evaluate the usefulness of HCO (7alpha-hydroxy-4-cholesten-3-one) serum concentrations as a diagnostic marker of bile acid malabsorption. The authors determined the reference range of HCO in 106 normal subjects (55 women, and 51 men, median age 40.2 years) and conducted a utility study in 23 patients with chronic diarrhea of unknown origin (13 women, and 10 men, median age 49.4 years). Bile acid malabsorption was identified by an increase of HCO in serum with a sensitivity of 90 percent and a specificity of 79 percent. The authors conclude that analyzing HCO in serum may serve as a novel,

simple, and sensitive method for detecting bile acid malabsorption in patients with chronic diarrhea of unknown origin. 2 figures. 21 references. (AA-M).

- **Diarrhea in the Critically Ill: Is it Causing or Complicating Severe Illness?**

  Source: Journal of Critical Illness. 13(5): 320-327. May 1998.

  Contact: Available from Cliggott Publishing Company. 55 Holly Hill Lane, Greenwich, CT 06831-0010. (203) 661-0600.

  Summary: Diarrhea can be either a primary disorder or it can complicate another disorder. In the first setting, dysenteric and cholera-like syndromes predominate. This article, the first in a series of two, focuses on the presentation and pathogenesis of various types of diarrhea in five clinical settings. The authors also explain how differences in epidemiology and physical findings yield clues to diagnosis and thus guide appropriate therapy. Watery diarrhea, the main characteristic of cholera-like disorders, is usually mediated by enterotoxins that alter fluid and electrolyte transport. Dysenteric syndromes are caused by inflammation or an invasive process involving the colon and occasionally the distal small intestine. Diarrhea can also complicate a variety of enteric and nonenteric systemic illness; in hospitalized persons, it can result from enteral feeding, medications, or infectious gastroenteritis. In immunosuppressed patients, diarrhea has become a frequent complication because of the advent of aggressive immunosuppressive regimens, improved survival of patients with malignant disease, and AIDS. One sidebar guides readers in differentiating causes of diarrhea in critically ill patients. 1 figure. 1 table. 20 references. (AA-M).

- **Diarrhea and Malabsorption in the Elderly**

  Source: Gastroenterology Clinics of North America. 30(2): 427-444. June 2001.

  Contact: Available from W.B. Saunders Company. 6277 Sea Harbor Drive, Orlando, FL 32821-9816. (800) 654-2452.

  Summary: Diarrhea from infectious organisms is common in the elderly and leads to frequent hospitalizations and a relatively high mortality (death) rate in this population. Diarrhea can be a disabling manifestation of several systemic disorders, including diabetes mellitus, and drug induced diarrhea is particularly common in advanced age. This article, from a special issue on gastrointestinal (GI) disorders in the elderly, addresses diarrhea and malabsorption in the elderly. Although the physiologic functions of intestinal digestion and absorption of macronutrients and most micronutrients are not decreased simply as a function of aging, malabsorptive diseases including chronic pancreatitis and celiac disease (gluten intolerance) are more common in the elderly than has been realized in the past. A particular potential cause of covert malabsorption of macro and micronutrients in older patients is bacterial overgrowth, which may occur in the absence of 'blind loops.' The impact of silent malabsorption on the nutritional health of older patients may be more severe than in the young. Physicians who care for elderly patients are cautioned to be alert to the possible presence of diarrhea and malabsorption. Older patients may not admit to having chronic diarrhea, particularly if they are also incontinent. When an intestinal infection and potential medication-induced gastrointestinal disturbances have been excluded, the differential diagnosis of diarrhea in the elderly is the same as in the young. In the elderly, micronutrient deficiency is a common presenting clinical picture; because the symptoms of malabsorption are covert, the diagnosis often is delayed and nutritional deficiencies are more common and more severe than in the young. 1 table. 102 references.

- **Diarrhea: Differentiating the Acute from the Chronic**

  Source: Patient Care. p.52-56. July, 2002.

  Contact: Available from Medical Economics. 5 Paragon Drive, Montvale, NJ 07645. (800) 432-4570. Fax (201) 573-4956.

  Summary: Diarrhea is a response of the bowel to infection, drugs, foods, or disease. Three factors can lead to the passage of unformed stools: an increase in intestinal fluid and electrolyte secretion (osmotic or secretory diarrhea), malabsorption of intraintestinal contents (due to damaged intestinal lining of the small bowel), and altered intestinal motility (dysmotility diarrhea). Proceeding directly to empiric or supportive therapy is often more practical than attempting to identify the cause of loose stools in some patients. This article focuses on differentiating acute and chronic diarrhea and how to determine which patients require diagnostic testing. Topics include the evaluation of acute and chronic diarrhea, and therapy for acute diarrhea. Stool examinations for ova and parasites may be indicated in patients when the illness originated during travel to high-risk areas or when illness persists longer than 2 weeks. Preventing dehydration is a major goal of therapy, and either over the counter (OTC) preparations or home remedies are often effective. Antibiotic therapy is generally not necessary for acute diarrheal episodes except when treatable parasites or some bacterial agents are known to cause the infection. 1 figure. 1 table. 4 references.

- **Chronic Diarrhea: Differential Diagnosis and Management**

  Source: Consultant. 41(1): 53-57. January 2001.

  Contact: Available from Cliggott Publishing Company. 55 Holly Hill Lane, Box 4010, Greenwich, CT 06831-0010. (203) 661-0600.

  Summary: Diarrhea that lasts longer than 4 weeks is considered chronic. This article reviews the differential diagnosis and management of patients with chronic diarrhea. Physicians are advised to first examine the patient for signs of fluid and nutritional depletion. Patients should be asked about exacerbating and alleviating factors, diet, drug use, recent travel, abdominal pain, weight loss, and stool characteristics. Blood in the diarrhea may implicate malignancy or chronic inflammatory bowel disease; food particles or oil in the stool may indicate maldigestion or malabsorption. Fecal leukocytes suggest inflammation, and eosinophilia is seen with neoplasms, allergy, collagen vascular diseases, parasitic infestation, and colitis. Stool analysis for fecal weight, osmotic gap, fat, occult blood, pH, and laxative abuse is often important in making the diagnosis. A 24 hour stool collection weighing less than 200 grams suggests incontinence, irritable bowel syndrome (IBS), or rectal disease, but not true diarrhea. Stool weight of more than 500 grams is rare with IBS; weight of less than 1,000 grams rules out pancreatic cholera syndrome. When the weight exceeds 2,000 grams per day, patients usually require intravenous fluids. Treatment options include bismuth subsalicylate, opiates, bulking agents, kaolin attapulgite, anticholinergics, and cholestyramine. 1 figure. 3 tables. 15 references.

- **Multiyear Prospective Study of the Risk Factors for and Incidence of Diarrheal Illness in a Cohort of Peace Corps Volunteers in Guatemala**

  Source: Annals of Internal Medicine. 132(12): 982-988. June 20, 2000.

  Contact: Available from American College of Physicians. American Society of Internal Medicine. 190 North Independence Mall West, Philadelphia, PA 19106-1572. Website: www.acponline.org.

Summary: Diarrheal illness is the most common medical disorder among travelers from developed to developing countries and is common among expatriate residents in developing countries. This article reports on a prospective longitudinal study undertaken in rural Guatemala to assess the risk factors for and incidence of diarrheal illness among Americans living in a developing country. The study cohort was 36 Peace Corps volunteers and the study included collection of daily dietary and symptom data for more than 2 years. The 36 volunteers in this study had 307 diarrheal episodes (mean, 7 per person), which lasted a median of 4 days (range, 1 to 112) and a total of 10.1 percent of the 23,689 person-days in the study. The incidence density (episodes per person year) was 4.7 for the study as a whole, 6.1 for the first 6 month period, 5.2 for the second 6 month period, and 3.6 thereafter. Statistically significant risk factors for diarrheal illness included drinking water whose source and quality were unknown (for example, the tap); eating food prepared by a Guatemalan friend or family; eating food at a small, working class restaurant; eating fruit peeled by someone other than a Peace Corps volunteer; drinking an iced beverage; and eating ice cream, ice milk, or flavored ices. Exposures generally were riskier if they occurred during travel elsewhere in Guatemala rather than in the person's usual work area. The authors conclude that diarrheal illness of mild to moderate severity continued to occur throughout Peace Corps service but decreased in incidence as length of stay increased. Various dietary behaviors increased the risk for diarrheal illness, which suggests that avoidance of potentially risky foods and beverages is beneficial. 1 figure. 3 tables. 25 references.

- **Escherichia Coli as a Cause of Diarrhea**

  Source: Journal of Gastroenterology and Hepatology. 17(4): 467-475. April 2002.

  Contact: Available from Blackwell Science. 54 University Street, Carlton South 3053, Victoria, Australia. +61393470300. Fax +61393475001. E-mail: Rob.Turner@blacksci-asia.com.au. Website: www.blackwell-science.com.

  Summary: Escherichia coli is the best known member of the normal microbiota of the human intestine and a versatile gastrointestinal pathogen (cause of disease). This article explores the role of E. coli as a cause of diarrhea. The varieties of E. coli that cause diarrhea are classified into named pathotypes, including enterotoxigenic, enteroinvasive, enteropathogenic, and enterohemorrhagic. Individual strains of each pathotype possess a distinct set of virulence-associated characteristics that determine the clinical, pathological and epidemiological features of the diseases they cause. In the article, the authors summarize the key distinguishing features of the major pathotypes of diarrhea-genic E. coli. Knowledge of the pathogenic mechanisms of these bacteria has led to the development of rational interventions for the treatment and prevention of E. coli induced diarrhea. The mainstay of antidiarrheal therapy is oral rehydration with sugar and electrolyte solutions. Importantly, patients suspected of being infected with these bacteria should not be treated with antibiotics because these may enhance toxin synthesis or promote its release from the bacteria with a consequent increased risk of hemorrhagic colitis. 4 figures. 4 tables. 59 references.

- **Serotonin-Transporter Polymorphism Pharmacogenetics in Diarrhea-Predominant Irritable Bowel Syndrome**

  Source: Gastroenterology. 123(2): 425-432. August 2002.

  Contact: Available from W.B. Saunders Company. 6277 Sea Harbor Drive, Orlando, FL 32887-4800. (800) 654-2452. Website: www.gastrojournal.org.

Summary: Irritable bowel syndrome (IBS) affects approximately 15 percent of adults, causes abdominal pain, discomfort, and altered bowel habits, and predominantly affects women. This article reports on a study of the use of serotonin (5HT) receptor antagonists in women with diarrhea- predominant IBS (DIBS). 5HT undergoes reuptake by a transporter protein (SERT). In the study, 30 patients (15 men, 15 women) with DIBS received 1 milligram twice a day of alosetron for 6 weeks; colonic transit was measured by scintigraphy at baseline and at the end of treatment. Results showed that SERT polymorphisms tended to be associated with colonic transit response; there was a greater response in those with long homozygous than heterozygous polymorphisms. Age, gender, and duration of IBS were not significantly different in the three groups (long, short, heterozygous). The authors conclude that genetic polymorphisms at the SERT promoter influence response to a 5HT antagonist in DIBS and may influence benefit to risk ratio with this class of compounds. 3 figures. 1 table. 57 references.

- **Toddler Diarrhea**

  Source: Practical Gastroenterology. 23(8): 39-40, 49-51. August 1999.

  Contact: Available from Shugar Publishing, Inc. 99B Main Street, Westhampton Beach, NY 11978. (631) 288-4404. Fax (631) 288-4435. E-Mail: info@practicalgastro.com.

  Summary: This article describes toddler diarrhea, a persistent, unexplained diarrhea that occurs in children aged 6 months to 3 years, and one of the most common forms of chronic diarrhea affecting children in their toddler years. Although these children typically remain medically well despite the frequent loose stools, the impact on the family emotionally, and sometimes financially due to missed work, can be substantial. Additionally, the chronic nature of the condition can be frustrating for the health care provider. Diagnostic considerations are reviewed and the recommended dietary changes that are used to treat this condition are outlined. Diagnosis of toddler diarrhea is based on the typical clinical features in the absence of signs suggestive of more significant pathology. Careful review of the child's growth, development, and physical exam should reveal a child who is thriving. One the diagnosis is established, treatment is based on eliminating contributing factors, limiting the possibility of carbohydrate malabsorption, and slowing the intestinal transit time. Fruit juices should be eliminated from the diet and water limited to 12 to 15 ounces per day. In general, an unrestricted diet and increase in dietary fat usually results in improved stool pattern within 2 weeks. 1 table. 15 references.

- **Are You Overlooking Oral Rehydration Therapy in Childhood Diarrhea?: It's Not Just for Use in Developing Countries**

  Source: Postgraduate Medicine. 104(4): 159-162, 165-166, 171. October 1998.

  Contact: Available from McGraw-Hill, Inc. 1221 Avenue of the Americas, New York, NY 10020. (612) 835-3222.

  Summary: This article discusses the indications for oral rehydration therapy in childhood diarrhea. In 1978, a prestigious medical journal declared that development of effective oral rehydration solutions might prove to be the most important medical advance of the century. Since then, according to estimates by the World Health Organization, the solutions have saved a million children a year worldwide. However, this method of treating diarrhea-induced dehydration has been virtually overlooked in the United States, where several hundred children still die from diarrhea. The authors propose that one reason for this is that physicians in developed countries have only limited exposure to serious dehydration and so are poorly informed on the principles of

intervention. The authors provide practical advice on assessing dehydration in children, administering initial and maintenance rehydration, and reinstituting feeding. Parents and caregivers can often provide simple, effective home care for infants and children with episodes of diarrhea through oral rehydration solutions and early return to normal feeding. The impact on physician visits, hospitalizations, and deaths related to diarrhea could be dramatic if United States physicians recommended oral rehydration solutions to parents and health care providers and advocated their inclusion on medical insurance formularies. 3 tables. 19 references. (AA-M).

- **Small Intestinal Mucosal Biopsy for Investigation of Diarrhea and Malabsorption in Adults**

  Source: Gastrointestinal Endoscopy Clinics of North America. 10(4): 739-753. October 2000.

  Contact: Available from W.B. Saunders Company. 6277 Sea Harbor Drive, Orlando, FL 32887-4800. (800) 654-2452 or (407) 345-4000.

  Summary: This article examines the clinical use of small intestinal biopsy for investigation of diarrhea or suspected malabsorption problems. The author stresses that the use of small intestinal biopsy for diagnosis in these conditions depends on an optimal interaction between the clinician endoscopist and the pathologist. This necessitates open and interactive communication between involved physicians and an appreciation for correct tissue handling and biopsy orientation in the endoscopy unit and the pathology laboratory. Classification of biopsy changes on the basis of architectural abnormalities in the small intestinal biopsy may be helpful in defining the diagnosis and include severe (flat) or variably severe (mild or moderate) abnormalities. For some small intestinal disorders that are characterized by diarrhea or malabsorption, the biopsy findings may be distinctive and lead to a specific diagnosis. For others, like celiac disease, the changes are less specific, and it has become better recognized that an increasing number of conditions can produce similar histopathologic changes. Definition of typical gluten sensitive biopsy changes in this disorder is critical. 1 table. 72 references.

- **Man with Acute Abdominal Pain and Diarrhea**

  Source: Consultant. 39(5): 1521-1522. May 1999.

  Contact: Available from Cliggott Publishing Company. 55 Holly Hill Lane, Box 4010, Greenwich, CT 06831-0010.

  Summary: This article offers a brief case report, with a discussion of appropriate treatment. The case was a 57 year old man who began experiencing acute abdominal pain with mild diarrhea 2 weeks after his return from New Mexico. The pain originated in the hypogastrium and involved the lower quadrant and the perineum. The diarrhea was characterized as two loose stools on the first day and two watery stools on the second day. The patient did not note blood or pus in the stools. The patient's history was unremarkable except for mild exercise induced asthma. His physical condition was normal except for very mild end expiratory wheezing and some diffuse abdominal tenderness with guarding but no rebound in the left lower quadrant. No masses were felt on abdominal palpation, and there was no hepatosplenomegaly. Blood studies revealed a mild leukocytosis; stool was trace heme positive. The author asks readers to choose from a set of five management options for the first 12 hours of handling this patient. The author stresses that the differential diagnosis for a patient who presents with abdominal pain and mild diarrhea is broad. The acute nature of the pain and the

lack of a toxic appearance in this case suggest either an infectious diarrheal disease or diverticulitis. A broad spectrum antibiotic (for instance, a fluoroquinolone such as trovafloxacin) with activity against the major gastrointestinal pathogens and the enteric flora found in diverticulitis is a good initial treatment for febrile patients with diarrhea of undetermined cause. The use of loperamide or narcotics as antimotility agents in patients with undiagnosed diarrhea and fever is a practice that should be discouraged. The authors stresses that physicians should consider surgery only if there is evidence of peritonitis or progression of disease with medical management. 4 references.

- **Dealing with Irregularity: Constipation, Diarrhea, Excessive Gas and Foul-Smelling Gas**

  Source: Digestive Health and Nutrition. 3(1): 16-20. January-February 2001.

  Contact: Available from American Gastroenterological Association. 7910 Woodmont Avenue, 7th Floor, Bethesda, MD 20814. (877) DHN-4YOU or (301) 654-2055, ext. 650. E-mail: DHN@gastro.org.

  Summary: This article offers strategies for dealing with problems of bowel irregularity, including constipation, diarrhea, excessive gas, and foul-smelling gas. The author notes that bowel habits vary greatly among individuals, so each person's perception of whether there even is a problem and how to deal with it best is different. The author stresses that too little fiber and liquid in the diet are by far the most common reasons for constipation among people living in western cultures. The fiber found in foods such as fruits, grains, and vegetables adds bulk to the stool, making it easier to move through the colon (large intestine). Liquids add both bulk and fluid to the stool. Exercise helps prevent constipation by maintaining energy levels and promoting intestinal activity. A number of pain medications; antidepressants; antacids that contain aluminum; diuretics; and antiinflammatory and antiseizure medications are some of the many medications that can contribute to constipation. Changes in routines can also cause irregularity. The author explores the role of aging as a cause of constipation. Laxatives are an effective remedy for constipation, but they should be used with caution. As with constipation, diarrhea means different things to different people. Bacterial and viral infections are the most common causes of acute diarrhea; food intolerance is another frequent cause of both diarrhea and gas. Regardless of the cause, diarrhea usually lasts only a few days and ends on its own without the need for medical attention. The author reviews the concerns regarding dehydration, which can be a consequence of diarrhea, particularly in children and in the elderly. Gas comes from two sources: swallowed air and the breakdown of certain undigested foods in the large intestine. Simple ways of reducing the gas from swallowed air include eating and drinking more slowly, not chewing gum, and having dentures properly fitted. For episodes of excessive or smelly intestinal gas, the use of a food diary may help identify the offending items. The author concludes by reiterating the importance of adequate fiber and fluid intake. The websites of four information resource organizations are listed.

- **Efficacy of Probiotic Use in Acute Diarrhea in Children: A Meta-Analysis**

  Source: Digestive Diseases and Sciences. 47(11): 2625-2634. November 2002.

  Contact: Available from Kluwer Academic Publishers. Customer Service Department, P.O. Box 358, Accord Station, Hingham, MA 02018-0358. (781) 871-6600. Fax (781) 681-9045. E-mail: kluwer@wkap.com. Website: www.wkap.nl. Distribution Centre, P.O. Box 322, 3300 AH Dordrecht, The Netherlands. 31 78 6392392. Fax: 31 78 6546474. E-mail: orderdept@wkap.nl.

Summary: This article reports on a study undertaken to review the effectiveness of probiotic use in reducing the duration of increased stool output in children with acute diarrheal illness. Studies eligible for review were limited to trials of probiotic therapy in otherwise healthy children less than 5 years old with acute-onset diarrhea. The main outcome variable was difference in diarrhea duration between treatment and control groups. The meta-analysis of 18 eligible studies suggests that coadministration of probiotics with standard rehydration therapy reduces the duration of acute diarrhea by approximately 1 day. In subsequent analyses limited to studies of hospitalized children, to double-blinded trials, and to studies evaluating lactobacilli, the pooled estimates were similar. The authors conclude that bacterial probiotic therapy shortens the duration of acute diarrheal illness in children by approximately one day. 2 figures. 1 table. 48 references.

- **Case Study: Antibiotic-Induced Acute Diarrhea**

  Source: Physician Assistant. 24(11): 56-58. November 2000.

  Contact: Available from Springhouse Corporation. Physician Assistant, P.O. Box 908, Springhouse, PA 19477. (215) 646-8700. Fax (215) 646-4399.

  Summary: This article reports the case of a 57 year old woman who presented to the emergency department with a 4 day history of abdominal cramps, nausea, and 2 to 3 episodes of watery diarrhea per day. She denied fever, vomiting, or bright red rectal bleeding. Her medical history was significant for seasonal allergic rhinitis, sinusitis, and depression. The differential diagnosis in this case included acute gastroenteritis, nonspecific abdominal pain, infectious diarrhea, giardiasis, Crohn's disease, ulcerative colitis, and antibiotic associated colitis (AAC). Because the clinical suspicion was high for AAC, the patient was given the diagnosis of presumptive Clostridium difficile enterocolitis and the cefpodoxime (a drug she was taking for the sinus infection) was stopped. She was started on metronidazole (Flagyl) 500 milligrams 3 times daily for 10 days and placed on a banana, applesauce, rice, and toast (BRAT) diet. At a family practice follow up appointment 2 days later, the patient was feeling much better. Laboratory studies showed presence of C. difficule toxins. The article describes this patient's need for a second course of drug therapy before complete resolution of the problem. The discussion section notes that antibiotic precipitated diarrhea is fairly common and may occur during the course of treatment or for several weeks after termination of the therapy. The first step for treating this disorder is discontinuing the probably offending antibiotics and starting treatment empirically with Flagyl or oral vancomycin. Antispasmodics are not recommended as they may worse the infectious process by prolonging contact between the organism and the intestinal mucosa. If the symptoms persist despite appropriate therapy, consultation with an infectious disease specialist is indicated. 3 references.

- **Reflux, Abdominal Pain, Diarrhea**

  Source: Patient Care. 33(7): 238-246, 249. April 15, 1999.

  Contact: Available from Medical Economics. 5 Paragon Drive, Montvale, NJ 07645. (800) 432-4570. Fax (201) 573-4956.

  Summary: This article reviews for primary care physicians the diagnosis and management of gastrointestinal reflux (heartburn), abdominal pain, and diarrhea. Although many cases can be managed routinely, some patients will require invasive procedures such as endoscopy or biopsy to rule out the possibility of serious disease. Other patients, perhaps even those with mild symptoms, may wish to undergo more

extensive diagnostic testing to alleviate their anxieties. Nonetheless, a complicated workup is an expensive and time consuming undertaking that is not needed in every case. The physician's task in evaluating the patient with these common gastrointestinal (GI) symptoms is to identify the threshold for referral. The author first reminds readers of the questions to focus on when taking the history, then notes that if symptoms are not long standing and no complications such as systemic disease appear likely, the remainder of the clinical evaluation is straightforward. The majority of patients with reflux can be managed empirically. They should be advised of lifestyle modifications that can contribute significantly to keeping them symptom free (avoiding late night snacks, elevating the head of the bed, avoiding foods that tend to cause esophageal irritation). The author then reviews the diagnosis of abdominal pain, again focusing on the patient history and the differentiation of acute versus chronic pain. The final section covers diarrhea, reminding readers of the most common causes of acute infectious diarrhea, the problem of chronic diarrhea, and inflammatory diarrhea (notably that due to Crohn's disease). 1 figure. 5 tables. 7 references.

- **Acute Infectious Diarrhea in Adults**

  Source: Patient Care. 33(15): 58-60, 63, 67, 70, 73-74, 76-77. September 30, 1999.

  Contact: Available from Medical Economics. 5 Paragon Drive, Montvale, NJ 07645. (800) 432-4570. Fax (201) 573-4956.

  Summary: This article reviews the diagnosis and treatment of acute infectious diarrhea in adults, focusing on determining when to provide supportive therapy versus a more detailed workup and targeted antibiotic therapy. Diarrhea can be defined as the passage of three or more unformed stools during a 24 hour period; the condition is acute if it persists for less than 14 days. The infectious agents that cause acute diarrhea are usually acquired by fecal oral transmission. Food may be contaminated by an infectious agent as a result of poor personal hygiene, a deficient sewage system, or by the use of inadequately purified water. The organisms most commonly isolated from patients with infectious diarrhea are Campylobacter jejuni, Salmonella species, diarrheagenic Escherichia coli, and Shigella species. Less frequent causes of diarrhea include Staphylococci, Bacillus cereus, Clostridium perfringens, Clostridium difficile, Vibrio species, and Yersinia species. The author discusses the special situation of diarrhea in patients with AIDS and briefly reviews the pathophysiology of diarrhea. For most patients with mild to moderate diarrhea, a diagnostic workup may not be necessary, and empiric, supportive treatment is usually sufficient. The author reviews the tests that may be used for more severe diarrhea, including fecal leukocyte testing, flexible sigmoidoscopy, stool culture, blood culture, ova and parasite examinations, and the C difficile toxin test. Fluid and electrolyte replacement usually are sufficient for mild diarrhea. Moderate diarrhea in adults or older children may be treated with bismuth subsalicylate, loperamide, or attapulgite. Antibiotic therapy may be appropriate for patients with febrile dysentery (fever is present), severe diarrhea with many fecal leukocytes (white blood cells in the feces), or with moderate to severe travelers' diarrhea. Specific antibiotic therapy is given when a treatable enteric pathogen is identified by stool or blood cultures. The article concludes with a section describing prophylaxis for travelers' diarrhea. 1 figure. 4 tables. 5 references.

- **Diarrhea in the Critically Ill: When and How to Use the Lab to Tailor Therapy**

  Source: Journal of Critical Illness. 13(6): 364-369. June 1998.

Contact: Available from Cliggott Publishing Company. 55 Holly Hill Lane, Greenwich, CT 06831-0010. (203) 661-0600.

Summary: This article reviews the diagnostic tests used to determine the cause of diarrhea and the therapy that can be used once the etiology is established. Fecal leukocyte testing and stool cultures are indicated for patients with fever or dysentery and for those hospitalized with (or for) diarrhea. Examination for parasites is warranted for persons whose diarrhea lasts more than a week, for those whose bloody stool has few leukocytes, for those who have recently traveled to developing countries or the Rocky Mountains, for homosexual men, and for infants in day care. Proctosigmoidoscopy is useful in persons with severe antibiotic associated diarrhea with an equivocal test for Clostridium difficile toxin and for those with amebiasis or idiopathic inflammatory bowel disease (IBD). Replacing fluid and electrolytes is the most important aspect of treatment, which may also include antimicrobial therapy or discontinuing medication that could be causing the diarrhea. Contraindications to oral rehydration therapy include intractable vomiting, sugar intolerance, abdominal distention, and ileus. Antibiotic therapy is recommended for patients with severe diarrhea, especially when it is associated with passage of bloody stools or fever. The treatment of choice is 250 mg of oral metronidazole every 6 hours for 10 days. Alternative therapy is 125 mg of oral vancomycin, 4 times a day for 10 days. 2 tables. 5 references. (AA-M).

- **Guidelines for Evaluating and Treating Chronic Diarrhea**

  Source: Consultant. 39(9): 2463-2464. September 1999.

  Contact: Available from Cliggott Publishing Company. 55 Holly Hill Lane, Box 4010, Greenwich, CT 06831-0010.

  Summary: This article summarizes strategies for evaluating and treating chronic diarrhea, a common problem that has many possible causes. A careful patient history taking is vital for identifying the possible causes of diarrhea. The author notes that although the physical examination may not help establish the cause of the patient's diarrhea, it can help establish the severity of the problem. Serum chemistry screening can help clarify the patient's fluid and electrolyte status and nutritional status, as well as identify any liver problems or dysproteinemia. A quantitative or a spot stool collection and analysis is useful to classify the type of diarrhea, which in turn may help identify its cause and indicate a management strategy. Stool tests include sodium and potassium concentrations in stool water, stool pH, fecal occult blood test, white blood cells, excess stool fat, and laxative screening. The author outlines additional testing that may be recommended for patients with chronic secretory diarrhea, chronic osmotic diarrhea, chronic inflammatory diarrhea, and chronic fatty diarrhea. The author recommends that empiric therapy should be administered under specific circumstances: as an initial measure before diagnostic testing; when diagnostic test results are inconclusive; or when the patient does not respond to treatment or when no treatment is available. Because adequate hydration is essential to successful treatment, some patients may require administration of oral hydration solutions. 1 table. 1 reference.

- **Travel Risks: Update on Traveler's Diarrhea and Other Common Problems**

  Source: Consultant. 42(14): 1778-1784. December 2002.

  Contact: Available from Cliggott Publishing Company. 330 Boston Post Road, Darien, CT 06820-4027. (203) 661-0600.

Summary: This article updates physicians on traveler's diarrhea and other common travel-related problems. The author notes that patients can greatly reduce the risk of traveler's diarrhea by drinking only bottled water and eating only hot foods prepared in sanitary conditions or peelable fruits and vegetables. Antibiotic prophylaxis for traveler's diarrhea is no longer routinely recommended; this approach should be reserved for patients who may have to consume food and beverages of questionable safety, those with reduced immunity, and those likely to experience serious consequences of illness. Adequate hydration is the first step in treating traveler's diarrhea. Drug therapy (loperamide or fluoroquinolones in adults and bismuth subsalicylate or azithromycin in children) can ameliorate symptoms and speed recovery. The article also discusses motion sickness, altitude sickness, travel medicine kits, and contraindications to air travel. 5 tables. 18 references.

- **Diarrhea and Tube Feeding**

  Source: Nutrition in Clinical Practice. 14(2): 83-84. April 1999.

  Contact: Available from American Society for Parenteral and Enteral Nutrition. 8630 Fenton Street, Suite 412, Silver Spring, MD 20910-3805. (301) 587-6315.

  Summary: Tube feeding (enteral nutrition) and diarrhea are often present together. The incidence of diarrhea in tube fed patients is 2 percent to 70 percent, with a higher occurrence in critically ill patients. This brief article offers a systematic method for the treatment of diarrhea in patients who are tube fed. The author notes that effective treatment of diarrhea must be initiated to minimize its metabolic, physical, and emotional complications. The primary goal is to reduce fluid, electrolyte, and nutrient losses through the stool. Intragastric feeds are associated with an increased incidence of diarrhea. Large caloric loads infused into the stomach promote colonic secretion of water, sodium, and chloride and, hence, reduce the absorptive capacity of the colon. If patients receiving gastric tube feeding develop diarrhea, they can be changed to a duodenal infusion. Fiber can be provided to safely promote fluid absorption in the colon during the diagnostic workup. Fiber should be added incrementally to reduce flatulence, abdominal distention (bloating), and constipation. The first step in identifying the etiology of diarrhea is to rule out enteric pathogens, such as Clostridium difficile. In addition, disease states such as diabetes, vitamin and mineral deficiencies, pancreatic enzyme deficiency, and malabsorption of fat and bile acids can contribute to diarrhea. Medications can be the reason for diarrhea in up to 61 percent of cases. Antibiotics, H2 receptor antagonists, antineoplastics, laxatives, antacids, and potassium and phosphate supplements are a few of the medications contributing to diarrhea. Sorbitol, an inactive ingredient in medications, is an active contributor to increased GI motility. If diarrhea continues despite treatment of enteric pathogens or disease related causes, antidiarrheal therapy, and medication adjustments, the enteral nutrition formula must be critically evaluated. One figure offers a patient care algorithm for treating diarrhea in tube fed patients. 1 figure. 4 references.

- **Hospital-wide Restriction of Clindamycin: Effect on the Incidence of Clostridium difficile-Associated Diarrhea and Cost**

  Source: Annals of Internal Medicine. 128(12 Pt 1): 989-995. June 15, 1998.

  Summary: Widespread use of antibiotics has been associated with increases in bacterial resistance and nosocomial infection. This article reports on a prospective, observational cohort study undertaken to characterize the impact of hospital-wide clindamycin restriction on the incidence of Clostridium difficile-associated diarrhea and on

antimicrobial prescribing practices. Clinical data on individual hospitalized patients with symptomatic diarrhea and data on antibiotic use were obtained from hospital pharmacy records. Hospital-wide use of antimicrobial agents was monitored. Isolates of C. difficile underwent antimicrobial susceptibility testing and molecular typing. Results showed that an outbreak of C. difficile-associated diarrhea was caused by a clonal isolate of clindamycin-resistant C. difficile and was related to increased use of clindamycin. A hospital-wide requirement that clindamycin be approved by an infectious disease consultant led to an overall reduction in use, a sustained reduction in the mean number of cases of C. difficile-associated diarrhea, and an increase in clindamycin susceptibility among C. difficile isolates. A parallel increase was noted in the use of and costs associated with other antibiotics with antianaerobic activity. The hospital realized overall cost savings as a result of the decreased incidence of C. difficile associated diarrhea. The authors conclude that hospital formulary restriction of clindamycin is an effective way to decrease the number of C. difficile infections. 3 figures. 1 table. 27 references. (AA-M).

Federally Funded Research on Diarrhea

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

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

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

- **Project Title: AGING AND THE HUMAN ANTIBODY RESPONSE TO C. DIFFICILE**

  Principal Investigator & Institution: Kyne, Lorraine; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

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

  Summary: A research program will be undertaken by the applicant, Lorraine Kyne, MD, MPH in the Division of Gerontology at the Beth Israel Deaconess Medical Center (BIDMC). The award will provide five years of mentored training and research enabling her to develop her potential to become an independent clinical investigator focusing on patient-oriented research. Dr Jeanne Y. Wei, Chief of Gerontology at BIDMC, Director of the Division on Aging at Harvard Medical School and Dr. Ciaran P. Kelly, Associate Physician in the Division of Gastroenterology, BIDMC, will serve as mentors. The research component will focus on an important iatrogenic, nosocomial condition which

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

affects predominantly older patients: Clostridium difficile-associated disease (CDAD). As the conventional antibiotic therapy of this condition is associated with a high relapse rate and the emergence of antimicrobial resistance, the long term goals of this project are to develop immunobiological products to prevent or ameliorate disease due to C. difficile and to test their efficacy in intervention studies in 'high risk' older persons. The specific aims of this project are; 1) to identify surrogate markers of immune protection against severe, prolonged or recurrent C. difficile **diarrhea** for use in future C. difficile active or passive immunization trials; 2) to explore the inter- relationship between the immune response to C. difficile, disease due to C. difficile and aging; and 3) to determine the clinical correlates of CDAD, in order to develop a clinical prediction rule which may be used to identify high risk individuals who may benefit from immunization or other preventative strategies. In addition to this project and scheduled meetings with Drs. Wei and Kelly, this award will include a formal research curriculum, including 1) Research ethics, 2) Clinical epidemiology, 3) Statistical analysis, 4) Clinical trials, 5) Aging research and 5) Laboratory techniques. The very substantial research, educational, and clinical resources of the Harvard Division on Aging and the BIDMC Gerontology and Gastroenterology Divisions will be committed to the applicant to ensure successful attainment of the goals of this award.

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

- **Project Title: ALANYL-GLUTAMINE AS ORAL REHYDRATION & NUTRITION THERAPY**

  Principal Investigator & Institution: Brito, Gerly A.; Scientist; Alglutamine, Llc 300 Preston Ave, 5 Flr Charlottesville, Va 22902

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

  Summary: (Scanned from the Applicant's Abstract): This resubmission with substantially sharpened goals and experimental design based on considerable new preliminary data now fully addresses the reviewers' questions. Building on promising preliminary data, we shall define the dose effects of alanyl-glutamine relative to glutamine, glucose, and other glutamine derivatives (including acetyl-glutamine) both in vitro and in vivo. Specifically, in vitro studies will examine intestinal epithelial repair, differentiation and prevention of apoptosis. In vivo studies will examine cyclic AMP and cyclic GMP-mediated secretory **diarrhea** induced by the toxins of V. cholerae and ST of E. coli, respectively, and the inflammatory, destructive enteritis induced by C. difficile toxin A or cytotoxic chemotherapy. Our overall goal for this first year is to have essential in vitro and in vivo data to support pilot human studies of alanyl-glutamine's effectiveness. Success will open commercial development of an effective new ORNT product for enhancing intestinal repair and absorptive function that could have relevance across a diverse range of human and animal applications. PROPOSED COMMERCIAL APPLICATION: NOT AVAILABLE

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

- **Project Title: ANIMAL MODEL OF ENTEROCYTOZOON BIENEUSI**

  Principal Investigator & Institution: Mansfield, Keith G.; Associate Professor of Pathology; None; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

  Timing: Fiscal Year 2001; Project Start 01-JAN-1998; Project End 31-DEC-2002

  Summary: (Adapted from applicant's abstract) E. bieneusi is a common infection in those with AIDS causing **diarrhea,** malabsorption and wasting in the terminal stages.

Inspite of its common occurance little is known regarding the basic biology, epidemiology and host immunity of this parasite. The applicants have been able to transmit and establish a persistant infection in SIV infected macaques using a parasite obtained from a human AIDS infection. Spontaneous infection with this parasite also occurs in macaques and is associated with hepatobiliary and intestinal disease. The applicant's hypothesis is that this parasite in macaques produces minimal clinical signs but establishes persistent **diarrhea** when the parasite is redistributed to selected areas of the hepatobiliary tree. Exacerbation of previously inapparent infection or acquisition of new infection during immunosuppression may result in expanded tissue distribution, dysfunction of the alimentary tract and progressive disease. In this proposal, the applicants propose to: 1) inoculate immunosuppressed monkeys with the parasite and determine distribution over time and its relationship to progressive suppression and functional changes, 2) to examine biological differences between rhesus amd human-derived microsporidia through evaluation of genetic markers and 3) develop methods for preparation of spores, production of antibody and quantification of parasites in tissue.

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

- **Project Title: ANTIBODY-BIOCIDE FUSIONS TO CONTROL CRYPTOSPORIDIUM**

  Principal Investigator & Institution: Imboden, Michael; Iogenetics, Llc Box 620128, 8137 Forsythia St Middleton, Wi 53562

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

  Summary: (provided by applicant): The goal of this research is develop therapeutic products for Cryptosporidium parvum which can be made at a scale and cost which are feasible for delivery to large populations of patients or individuals at risk, as may be necessary in countering bioterrorism, or in protecting field-deployed armed forces. Our approach is to develop recombinant neutralizing monoclonal antibodies, and fusion proteins that genetically link monoclonal antibodies to parasiticidal proteins (biocides) which neutralize C. parvum sporozoites and merozoites. We will use a proprietary retrovector gene transfer technology to insert multicistronic gene constructs for the monoclonal fusion product candidates into cell culture. Following identification of products effective in vitro and in mouse models, we will scale up production in cell culture and by creation of transgenic cattle that express the monoclonal antibodies and fusion proteins in their milk and test anti-cryptosporidial efficacy in neonatal mice and pig models. Transgenic expression will enable manufacture of anti-cryptosporidial therapeutics economically and on a large scale. In addition to biodefense applications, the technology developed will also have important dual-use application in treatment of opportunistic infections with C. parvum and traveler's **diarrhea,** and in veterinary use to reduce the environmental reservoir of infection.

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

- **Project Title: APOPTOSIS IN SHIGELLA INFECTIONS**

  Principal Investigator & Institution: Basilico, Claudio; Professor and Chairman; Microbiology; New York University School of Medicine 550 1St Ave New York, Ny 10016

  Timing: Fiscal Year 2001; Project Start 01-MAR-1996; Project End 31-MAY-2005

  Summary: Shigellae are the etiological agents of bacillary dysentery, a severe form of **diarrhea** that is often fatal in infants. Shigellosis is an acute inflammatory disease. Here

we propose to investigate the role of apoptosis in the initiation of inflammation. We have demonstrated that Shigella induces apoptosis in macrophages in vitro and in vivo. Shigella first invades cells and then escapes from the phagocytic vacuole into the cytoplasm. In the cytoplasm, Shigella secretes the plasmid-encoded virulence factor Invasion Plasmid Antigen (Ipa) B which is necessary to induce cell death. IpaB binds to caspase (Casp)-1, a host cysteine protease that is required for Shigella induced apoptosis. Apoptosis mediated by Casp-1 appears to be pro- inflammatory in Shigella infections, since Casp-1 proteolytically activates the cytokines pro-Interleukin (IL)-1beta and pro-IL-18. Macrophages infected with Shigella release mature IL-1beta and IL-18. Furthermore, casp-1 knock-out mice do not mount an acute inflammation in response to Shigella infection. In vivo, some apoptotic cells are localized to regions of the lymphoid follicle where Shigella is not detectable. This difference in distribution suggested that Shigella possesses a second cytotoxic molecule, not IpaB, that can diffuse within infected tissue. We identified the novel diffusible cytotoxic activity in Shigella culture supernatants as Bacterial Lipoproteins (BLP). We also demonstrated that BLP activates both apoptosis and the host cell transcription factor Nuclear Factor - kappa B (NF-kappaB) through the Toll Like Receptor (TLR)2. In this application we propose to further understand the significance of apoptosis in Shigella infections. More specifically we will determine: (1) the role of Casp-1 activated cytokines in acute inflammation and whether apoptosis is required for the release of mature IL-1beta and IL-18 and (2) the signal transduction pathway activated by TLR2 after treatment with BLP and the role of BLP and TLR2 in vivo.

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

- **Project Title: BOVINE SPECIFIC VIRULENCE FACTORS OF S TYPHIMURIUM**

  Principal Investigator & Institution: Baumler, Andreas J.; Associate Professor; Medical Microbiol & Immunology; Texas A&M University Health Science Ctr College Station, Tx 778433578

  Timing: Fiscal Year 2001; Project Start 15-JUN-1999; Project End 31-MAY-2003

  Summary: (Adapted from the Applicant's Abstract): Salmonellosis is the most frequent food-borne illness in the US. The recent emergence of multiple antibiotic-resistant S. typhimurium strains, such as definitive phage type 104 (DT104) has illustrated that the use of antibiotics will no longer combat salmonellosis effectively in the future. In order to devise alternatives to antibiotic therapy for the control or prevention of Salmonella infections, an understanding of the fundamental factors that Salmonella uses to cause infection and disease is needed. Little is known about genes allowing S. typhimurium to infect cattle, an important meat source in the US. The proposed research will characterize bovine virulence factors of S. typhimurium which will facilitate the development of improved strategies for prevention and treatment of infection. This research will also establish a new animal model for the study of human diarrheal disease caused by Salmonella. Overall project goals and supporting objectives: (1) Analysis of the adherence mechanisms which contribute to host adaptation. (2) Analysis of the role of the invasion associated type III secretion system in host-adaptation and **diarrhea.** Plans to accomplish project goals: The investigators have identified two virulence factors which contribute specifically to disease in cattle. One, a putative adhesin, will be characterized to determine its role in colonization of bovine intestine. The second factor is a secretion system which is specifically required to cause **diarrhea** in calves. They will determine the identity of the secreted proteins and study their role in causing **diarrhea.**

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

- **Project Title: BUILDING A 3-DIMENSIONAL MODEL OF THE PORE OF CFTR**

  Principal Investigator & Institution: Mccarty, Nael A.; Associate Professor; School of Applied Biology; Georgia Institute of Technology 225 North Ave Nw Atlanta, Ga 30332

  Timing: Fiscal Year 2001; Project Start 15-SEP-2001; Project End 31-AUG-2006

  Summary: The CFTR protein forms a chloride ion channel in the plasma membranes of many epithelial cells, including cells of the kidney and gut. Mutation of the gene encoding CFTR is the primary defect in Cystic Fibrosis (CF), the most common lethal, autosomal recessive disease among Caucasians, affecting approximately 30,000 Americans. Alteration in CFTR function also plays an important role in the pathophysiology of secretory **diarrhea** and polycystic kidney disease (PKD). The basic mechanisms of permeation in this channel are not clear. It is not known which portions of the protein contribute to forming the pore, and which amino acids in those domains are involved in the biophysical processes of ion permeation. The long-term objective of this laboratory is to determine the mechanisms of permeation in CFTR. For this proposal, Specific Aim number 1 is to determine the oligometric structure of the functional CFTR channel. Specific Aim number 2 is to identify transmembrane (TM) helices that line the pore, by localization of binding sites for open-channel blockers. Specific Aim number 3 is to identify groups of amino acids that serve as determinants of anion selectivity. The proposed approach relies upon the use of molecular biological techniques (site-directed mutagenesis) combined with expression in Xenopus oocytes and quantitative biophysical assays. The working hypothesis is that the pore is lined by TM domains 5, 6, 11, and 12. To achieve these goals, whole-cell and single-channel currents will be measured to determine the kinetics of two structurally-distinct classes of pore-blocking molecules, and to determine whether their binding domains contribute to the permeation pathway. Structural elements that contribute to the architecture of the pore will be defined by comparing the ability of wildtype and mutant channels to interact with open-channel blockers. Previous studies from this laboratory have shown that blocker kinetics are highly sensitive to the structure of the pore. A region within TM6 has been identified that is critical for discrimination between different anions. This region also appears to lie close to the binding sites for pore-blocking molecules. To accurately describe the structure of this region of the channel, it is necessary to consider to contributions made from portions of the channel other than TM6. These studies will be guided by a three- dimensional model of the pore, proposed in the application, which takes into account the experimental data for TM domains 5, 6, 11, and 12. This approach hypothesizes that multiple helical domains contribute both to the binding sites for drugs and to the determinants of selectivity in the channel. A specific subset of residues that may determine the biophysical features of permeation is proposed. Testing the importance of these residues will allow the construction of a detailed map of the conduction pathway. An improved understanding of the function of this channel will aid in the design of novel therapies for Cystic Fibrosis, secretory **diarrhea,** and polycystic kidney disease.

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

- **Project Title: C. DIFFICILE TOXIN MEMBRANE TEST WITH MAGNETIC PARTICLES**

  Principal Investigator & Institution: Zheng, Limin; Techlab, Inc. 1861 Pratt Dr, Ste 1030 Blacksburg, Va 24060

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

Summary: (provided by applicant): The use of paramagnetic particles (PMP) and their detection in a magnetic assay reader (MAR) represent a new "platform" technology that is adaptable to lateral flow membrane systems. In preliminary studies, the new technology is capable of delivering 3 to 4 logs increased sensitivity over existing lateral flow technologies that use immunogold or enzyme-tagged antibodies. We propose to develop a new rapid lateral flow system for Clostridium difficile toxins A and B using this technology. C. difficile is an excellent candidate to evaluate the technology. This anaerobic pathogen is the leading cause of nosocomial **diarrhea** and colitis in industrialized countries. Although the current antibody-based tests for C. difficile are more rapid than the tissue culture assay, which is considered the gold standard, they do not offer the same level of sensitivity. In Phase I, we will optimize the conditions needed to develop a PMP test for the toxins of C. difficile. We will optimize the PMP conjugation process, test formatting with separation membrane and capture line processes, evaluate stability, and develop a fecal sample diluent. A prototype device will be developed and we will initiate studies to evaluate performance characteristics. In addition, we will develop antibodies for the detection of iota toxin, a newly recognized C. difficile toxin. Phase II will be a natural extension of Phase I. The technology for producing the device will be transferred to a GMP facility, and we will evaluate GMP produced devices through in-house and on-site studies. Data will be collected and compiled, and 510(k) documents will be prepared. Using the PMP lateral flow technology platform that we will evaluate in Phase I, we will also develop a diagnostic C. difficile panel test, which will be useful for epidemiological and surveillance studies of C. difficile disease. In addition, we will develop a clinical diagnostic panel test for antibiotic associated **diarrhea** (AAD), including a PMP-based test for C. perfringens enterotoxin, another cause of AAD. The technology developed in this project will be widely applicable for the development of new highly sensitive stool antigen tests.

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

- **Project Title: CELIAC DISEASE IN OSTEOPOROSIS**

  Principal Investigator & Institution: Stenson, William F.; Professor; Barnes-Jewish Hospital Ms 90-94-212 St. Louis, Mo 63110

  Timing: Fiscal Year 2001; Project Start 15-JUN-2000; Project End 31-MAY-2005

  Summary: (Abstract of the application) There is compelling evidence that the prevalence of celiac disease in the general population in the United States is higher than is generally appreciated and that patients with the symptoms classically associated with celiac disease, primarily **diarrhea** and weight loss, form a relatively small portion of the total celiac population. Some patients with celiac disease have medical problems associated with the malabsorption of specific nutrients without having problems with **diarrhea** and weight loss. Celiac disease is associated with the malabsorption of calcium and vitamin D resulting in osteoporosis. Although the prevalence of osteoporosis in the population of patients with celiac disease is known to be increased compared to the prevalence in the general population, the contribution of celiac disease to osteoporosis in the general population and the prevalence of celiac disease in the population of patients with osteoporosis are unknown. The central hypotheses of this proposal are: 1. The prevalence of celiac disease in the population of patients with osteoporosis is significantly increased above that of the general population. 2. Management of osteoporotic patients with celiac disease would be facilitated by the diagnosis and treatment of their celiac disease. These two premises taken together would justify a public health recommendation for screening patients with osteoporosis with serological tests for celiac disease. We have the unique resource of a Bone Health Clinic with a

database that includes more than 2,000 individuals with osteoporosis as well as an even larger number of patients with normal bone density. In addition, the Bone Health Clinic sees more than 750 new patients per year of which 50% have osteoporosis. We propose to use the resources of our Bone Health Clinic to test this hypothesis. We have two Specific Aims: 1. To define the prevalence of celiac disease in a population of patients with osteoporosis and to compare the prevalence in a case control group of individuals with normal bone mass indices. This Specific Aim will be pursued using patients from the Bone Health Clinic database that will already have been defined as having osteoporosis and new patients accrued to the Bone Health Clinic. If the prevalence of celiac disease in the osteoporotic population is high enough one could justify a public health recommendation that all patients with osteoporosis undergo serologic screening for celiac disease. Studies under this Specific Aim will also allow recommendation for which sequence of serologic tests is most likely to be helpful in identifying patients with osteoporosis who also have celiac disease. 2. To determine if there are any significant differences in the clinical histories, laboratory studies or response to therapy between the populations of newly diagnosed and previously untreated osteoporotic patients with and without celiac disease. Specific studies will include: a. We will compare the population of patients with osteoporosis and celiac disease with the population of patients with osteoporosis without celiac disease in terms of their clinical characteristics and biochemical parameters determined at the time of diagnosis. b. We will compare patients with osteoporosis and celiac disease with patients with osteoporosis without celiac disease in terms of their response to therapy. Patients with osteoporosis without celiac disease will receive calcium and vitamin D for one year, whereas patients with osteoporosis and celiac disease will receive calcium, vitamin D and a gluten-free diet for one year. At the end of the year of therapy, bone mass indices will be repeated and the response to the therapy of the two groups will be compared.

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

- **Project Title: CLONIDINE TREATMENT FOR NEONATAL ABSTINENCE SYNDROMEN**

  Principal Investigator & Institution: Gauda, Estelle B.; Associate Professor; Pediatrics; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-JUL-2006

  Summary: (provided by applicant): In the United States, as many as 20,000 babies a year are born to opioid ("narcotic") addicted mothers. Like their mothers, these infants are opioid dependent. Following birth, the infant is removed from its opioid source, inducing a withdrawal syndrome in these infants. Withdrawal symptoms in newborns include vomiting, **diarrhea,** poor feeding, tachycardia, hypertension, diaphoresis, restlessness, insomnia, irritability, tremors, clonus, hyperphagia with poor growth and acidosis, reversible neurologic abnormalities, and even seizures. This complex of signs and symptoms is referred to as neonatal abstinence syndrome (NAS). Reinstitution of opioids followed by a slow tapering protocol is currently the standard of care, necessitating prolonged hospitalization from weeks to months. Clonidine is a non-narcotic central alpha2-adrenergic receptor agonist that blocks the effects of over-excitation of the sympathetic nervous system and is an approved treatment for opioid withdrawal in adults. We currently have a physician sponsored IND (#63,781) to study the effect of clonidine as adjunct therapy to opioids for the treatment of NAS. This proposal will test the hypothesis that combination therapy of clonidine and opioids is 1) safe and efficacious, 2) allows reduced amount of opioid drug use, and 3) results in shorter time of treatment and hospitalization. This will be accomplished in a

randomized, placebo controlled double blind clinical trial comparing diluted tincture of opium (DTO) combined with a placebo (control) vs. DTO combined with clonidine. Additional sub-studies include determination of 1) pharmacokinetics and pharmacodynamics of DTO and clonidine in the enrolled cohort and 2) further safety evaluation by evaluating developmental outcome on the Bayley Scale of Infant Development (BSID) at 6 and 12 months of age. Pharmacokinetics will be determined by measuring serum concentrations of clonidine and morphine and analyzing volume of distribution, elimination half-life and clearance. These results will have important clinical implications and may change the standards of care not only for management of infants with severe NAS, but also for the management of infants and children, after long-term iatrogenic opioid exposure for instance following prolonged analgesia for mechanical ventilation or multiple operations.

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

- **Project Title: CONTRACTILE SIGNAL TRANSDUCTION IN ULCERATIVE COLITIS**

  Principal Investigator & Institution: Cao, Weibiao; Rhode Island Hospital (Providence, Ri) Providence, Ri 02903

  Timing: Fiscal Year 2003; Project Start 10-JAN-2003; Project End 31-DEC-2004

  Summary: (provided by applicant): Ulcerative colitis is a chronic inflammatory condition affecting the large bowel: Although it is most frequent in the rectosigrnoid area, it may involve the whole colon. Inflammation in ulcerative colitis is histologically limited to the mucosa, and its effects have been better characterized in the superficial than in the deeper layers such as muscularis propria. Inflammation, however, may affect the muscle layer, leading to motor dysfunction, which contributes to key clinical symptoms, including **diarrhea,** constipation, and crampy abdominal pain. To define inflammation, associated changes in motor function we will examine the circular muscle from the sigmoid colon from patient with active ulcerative colitis and compare it with muscle from disease-free margins of histologically normal colon tissue from cancer resections. The sigmoid is most often involved and frequently resected, and this avoids variations associated with different anatomical locations of the disease. In preliminary experiments, we find that inflammatory mediators such as interleukin-1beta and hydrogen peroxide are present in the muscularis propria. Our central hypothesis is that inflammatory mediators, first produced by inflammatory cells in the mucosa, may induce production of additional mediators by the target cells themselves, and that in time the muscularis propria becomes affected leading to motor disturbances. We therefore propose to: A) Define inflammation-induced changes in contractile signal transduction pathways of human sigmoid colon. B) Test the effect of selected inflammatory mediators, known to be present in ulcerative colitis mucosa, to determine their individual contribution to the observed changes in colonic motor function. C) Determine whether inhibition of selected inflammatory mediators may reverse inflammation-mediated changes in colonic motor function. Examining the relationship between inflammatory mechanisms and changes in motor function may help in understanding the functional disturbances associated with ulcerative colitis and identifying new targets for therapeutic intervention.

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

- **Project Title: CONTROL OF COLONIC MOTILITY IN HEALTH AND DISEASE**

  Principal Investigator & Institution: Sarna, Sushil K.; Professor; Surgery; Medical College of Wisconsin Po Box26509 Milwaukee, Wi 532264801

Timing: Fiscal Year 2001; Project Start 01-APR-1984; Project End 31-DEC-2001

Summary: Abnormal colonic motility in idiopathic human ulcerative colitis as well as in animal models of colonic inflammation is characterized by the suppression of rhythmic phasic contractions, decrease n tone and increase in the frequency of giant migrating contraction (GMCs). These motility abnormalities play a key role in producing the symptoms of **diarrhea,** urgency of defecation and abdominal cramping. The cellular mechanisms for the generation of tone, phasic contractions and GMCs in the colon are not known. The first aim of this proposal is to investigate the roles of specific signal transduction pathways in the generation of tone and stimulation of phasic contractions in the colon. The second aim is to determine how these signal transduction pathways are modulated by the inflammatory response to suppress the tone and phasic contractions. Key intracellular messengers including cytosolic free Ca2+, Ca2+ efflux from intracellular stores, IP3, DAG and PKC, will be measured to support the physiological and pharmacological observations. Patch clamp studies will be done on freshly dissociated cells and circular muscle strips taken from normal and inflamed canine colon. Extensive in vivo and in vitro data are available from this species to help in the interpretation of our data and relating it to clinical diseases. Mucosal exposure to ethanol and acetic acid will be used to induce inflammation. The motility abnormalities in this model are similar to those reported in human ulcerative colitis. An understanding of the differences n signal transduction pathways that generate tone and stimulate phasic contractions may present the opportunity to regulate each type of contraction separately from the other. In inflammatory bowel disease and other forms of gut inflammation it would be desirable to selectively stimulation phasic contractions and tone to minimize **diarrhea,** urgency of defecation and abdominal discomfort.

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

- **Project Title: COORDINATION OF MOTILITY AND SECRETION**

  Principal Investigator & Institution: Cooke, Helen J.; Professor; Pharmacology; Ohio State University 1800 Cannon Dr, Rm 1210 Columbus, Oh 43210

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

  Summary: Enteric infections and inflammation are often associated with disturbances in gastrointestinal motility and secretion. One of the common symptoms is **diarrhea.** Structural and functional alterations, which occur in the enteric nervous system and interstitial cell networks in these disease states, may lead to long term disturbances in intestinal function. In order to gain an understanding of how the neural networks are programmed to regulate muscle contraction and secretion, the following specific aims will be addressed in the colon of normal guinea pigs. The first is to determine the neural pathways that coordinate muscle contraction with secretion when the stimulus is mucosal stroking. Proposed studies focus on the afferent and efferent limbs of the reflex. They include determination of the role of endogenous and exogenous 5-HT in coordinating muscle contraction and secretion, on pharmacological drugs to evoke or uncouple synaptic transmission between submucosal and myenteric ganglia and on the neurochemical and electrophysiological identity of intrinsic afferent neurons. The second aim is to determine the neural pathways coordinating repetitive contraction and repetitive secretion when the stimulus is histamine. Planned studies include identification of the cellular structures mediating histamine's effects and analysis of the spread of excitation through neural and interstitial cell networks. Methodologies to be used include a brush mechanism, in an in vitro whole tissue preparation, to activate intrinsic neural reflexes while recording strain gauge tension and short circuit current simultaneously. These methods will complement in situ laser confocal imaging of living

tissues and will be combined with electrophysiology, morphology, immunohistochemistry and retrograde labeling of neurons to obtain a spatial analysis of calcium signals throughout the enteric nerve plexus and network of interstitial cells. These novel approaches are expected to provide new information on interactions of the enteric nervous system and interstitial cell network with muscle and epithelial cells. These studies should provide new insights into integration of two diverse functions, muscle contraction and epithelial secretion, necessary for propelling and lubricating the intestinal contents. Furthermore, they may identify potential targets for the action of therapeutic drugs used in the treatment of **diarrhea.**

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

- **Project Title: CORE--ADMINISTRATIVE & SPECIMEN AND DATABASE MAINTENANCE**

  Principal Investigator & Institution: Morrow, Ardythe L.; Associate Professor; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

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

  Summary: This core is in charge of the overall administration of the four projects that form this PPG. Many of the investigators have been associated with the PPG for as long as 15-23 years. Indeed, the strength of this PPG is the long-standing interaction of the PI's of the individual projects and their respective teams. The close collaboration among the various projects has enabled the development and testing of new hypotheses in the field of protection of the newborn against infection by his/her mother's milk. The core provides administrative support to the 21 investigators in the various projects. This support includes: 1. Maintenance of the specimens collected from the 1987-1991 and current (1998-2003) cohorts of 622 mother/infant pairs from the studies conducted in Mexico. In addition, the PPG now includes cores and projects in Cincinnati, Mexico, Boston and Houston. 2. Maintenance of the database generated by the PPG from 1987 on. 3. Maintenance of close links with other specialized cores: Molecular Biology (Cincinnati), Glycobiology (Boston), Epidemiology and Biostatistics (Cincinnati), and the Mexico Core. 4. Supervision of the clinical study sites in Mexico and Cincinnati.

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

- **Project Title: CPT11 ACTIVATION BY CARBOXYLESTERASES IN COLON CANCER**

  Principal Investigator & Institution: Bosron, William F.; Professor; Biochem and Molecular Biology; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, in 462025167

  Timing: Fiscal Year 2002; Project Start 15-FEB-2002; Project End 31-JAN-2004

  Summary: This is a R21 developmental grant application in response to NCI PA- 01-010, "Exploratory studies in cancer detection, prognosis and prediction." The overall goal is to produce a CPT-11 (Irinotecan) carboxylesterase assay that could be used to predict treatment outcome and/or toxicity for patients on CPT-11 therapy for colorectal cancer. CPT-11 is a semi-synthetic pro-drug that is activated by hydrolysis in vivo to SN-38. SN-38 is a potent inhibitor of topoisomerase I and therapy inhibits cell growth. Another important metabolite called APC is also hydrolyzed to SN-38. The specific carboxylesterases responsible for the hydrolytic activation of CPT-11 and APC to SN-38 are not known. Two human carboxylesterases, hCE-1 and hCE-2 is highly expressed in intestine, which may be related to the major toxic complication of CPT- 11 therapy, **diarrhea.** Our hypothesis is that the tissue and cell-specific expression of CPT-1 and

APC carboxylesterases may be an important determinant of the therapeutic outcome and toxicity associated with the APC carboxylesterases. Analysis of carboxylesterase-like genes in GenBank and preliminary observations in tumor cell lines suggest that there may be other carboxylesterases that could catalyze the hydrolysis of CPT-11 and APC. Proteomics and PCR methodologies will be used to screen for carboxylesterases and kinetic analysis with CPT-11 and APC as substrates will be performed with isolated or expressed enzymes. The second scientific aim of the grant is to develop and validate assays employing activity assays, gel electrophoresis or PCR methodologies for analysis of CPT-11 carboxylesterase expression in tumor and normal colon tissue from patients treated with CPT-11. A pilot study will be performed with tumor and normal tissue collected from patients at the Indiana University Cancer Center who presented with metastatic disease at diagnosis. After surgery the patients will be treated with 5-fluorouracil, Leucovorin and CPT-11. The response to CPT-11 therapy and associated toxicity will be compared to carboxylesterase expression in tumor and normal colon tissue. If there is a positive correlation, a future multi-institutional study will be proposed.

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

- **Project Title: CRYPTOSPORIDIUM PARVUM GENOME SEQUENCING PROJECT (MINN)**

  Principal Investigator & Institution: Abrahamsen, Mitchell S.; Assistant Professor; Veterinary Pathobiology; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

  Timing: Fiscal Year 2001; Project Start 15-APR-2000; Project End 31-MAR-2003

  Summary: Description (Adapted from applicant's abstract): Cryptosporidium parvum is a well-recognized cause of **diarrhea** in humans and animals throughout the world, and is associated with a substantial degree of morbidity and mortality in patients with the acquired immunodeficiency syndrome (AIDS). At the present time, there is no effective therapy for treating or preventing infection with C. parvum. This is primarily due to a lack of understanding of the basic cellular and molecular biology of this pathogen in terms of virulence factors, genome structure, gene expression, and gene regulation. With the recent advances in high-throughput automated DNA sequencing capabilities, large-scale genomic sequencing has become a cost-effective and time-efficient approach to understanding the biology of an organism. This is in stark contrast to the cost and time associated with single gene studies. Our preliminary studies on the genetic structure and genome organization of C. parvum have led us to formulate the hypothesis that genome sequencing will prove to be an efficient and cost-effective method for gene discovery for this eukaryotic pathogen. The following specific aims are proposed: 1) Generate and "end sequence" a random small-insert C. parvum genomic library; 2) Generate and "end sequence" large-insert (15-20 kb) C. parvum genomic libraries to provide a scaffold for sequence assembly; 3) Assemble sequences using Phred/Phrap/Consed software and assign contigs to specific chromosomes; 4) Finish sequencing of the genomic sequences; 5) Annotate/analyze the assembled completed genomic sequence to identify and characterize genes and structural features of the C. parvum genome. These studies will increase our basic understanding of the cellular and molecular biology of C. parvum in terms of gene and genome structure, and will identify key metabolic and pathophysiologic features of the organism for future development of sate and effective strategies for prevention and treatment of disease. Importantly, our preliminary data demonstrates that (a) we have all the necessary

reagents and expertise required for completion of the proposed studies and (b) our ability to conduct large-scale analysis of the C. parvum genome.

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

- **Project Title: DEVELOPMENT OF ROTAVIRUS DNA VACCINES**

  Principal Investigator & Institution: Herrmann, John E.; Professor; Medicine; Univ of Massachusetts Med Sch Worcester Office of Research Funding Worcester, Ma 01655

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

  Summary: (Adapted from Applicant's Abstract) The goal of our studies is to develop and test rotavirus DNA vaccines in mice and gnotobiotic pigs that will provide the basis for development of human rotavirus DNA vaccines. Rotaviruses are the major cause of severe acute **diarrhea** in children, resulting in an estimated 870,000 deaths per year, and current vaccines have not been effective in developing countries where the need is the greatest. We have shown that protective immunity in mice was obtained by parenteral inoculation of DNA vaccines encoding rotavirus proteins and by oral administration of rotavirus DNA vaccines encapsulated in poly (lactide-co-glycolide) (PLG) microparticles. We will evaluate protection generated by DNA vaccines in mice and in gnotobiotic or rotavirus antibody-free conventional pigs, the only animal models that can be clinically infected with human rotaviruses. Immunization will be by oral administration or by intramuscular inoculation with VP2, VP4, VP6 and VP7 DNA vaccines. VP7 is the major neutralization antigen of the outer capsid and the VP7 (G) serotypes 1-4 are the basis of the live, attenuated rhesus-human reassortant tetravalent rotavirus vaccine. To test the possibility of preparing VP7 DNA vaccines derived from human and simian rotaviruses, we will prepare one VP7 DNA vaccine from simian SA-11 rotavirus (for testing against EDIM rotavirus in the mouse model; EDIM and SA-11 are both G serotype 3 viruses), and one VP7 DNA vaccine from human Wa rotavirus (G serotype 1) for testing against Wa rotavirus challenge in gnotobiotic pigs. Mucosal and systemic immune responses to DNA vaccines will be examined in an adult mouse model and in gnotobiotic pigs or rotavirus antibody-free conventional pigs. The antibodies and specific isotypes induced by each DNA vaccine will be examined for virus neutralizing activity and epitope specificity. Cell-mediated immune responses to be examined in the mouse model include cytotoxic T cell responses and specific T helper cell subsets induced. Studies in pigs will include quantitating lymphoproliferative (T cell) and antibody secreting cell (B cell) responses from mucosal and systemic tissues. The need for improved rotavirus vaccines is a continuing one. Immunization with DNA vaccines that express specific rotaviral proteins offers a new approach to vaccination against rotaviruses and may provide the next generation of rotavirus vaccines.

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

- **Project Title: DIARRHEAL DISEASE--A PHYSIOLOGIC APPROACH TO TREATMENT**

  Principal Investigator & Institution: Donowitz, Mark; Leboff Professor of Medicine; Medicine; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2001; Project Start 01-JUN-1988; Project End 31-MAR-2003

  Summary: This proposal deals with several aspects of signal transduction which are unique to epithelial tissues. Differences in the signaling pathways in the apical and basolateral membranes (BLM) of intestinal epithelial cells are explored which are initiated by BLM signals generated by EGF (acting by a tyrosine kinase receptor), and carbachol (acting by a G- protein linked receptor). Both regulate the ileal apical

membrane neutral NaC1 absorptive process and its component brush border (BB) Na/H exchanger. NHE3 with EGF causing stimulation and carbachol inhibition. A major topic of this proposal deals with how signals generated from the BLM are focused on BB processes, in this case on BB Na/H exchange. We hypothesize that this is achieved by BB signaling complexes that involve the long cytoplasmic C-terminus of the transport protein being regulated, NHE3. We propose to build on our novel observation that there are BB signaling complexes which contain NHE3; the tyrosine kinases c-Src and c-Yes; two PIP2 utilizing enzymes, PI 3-kinase and PI- PLCgamma; and two microvillus cytoskeletal components, villin and ezrin with EGF and carbachol acting by different members of these complexes. The insights in signal transduction to be gained from these studies will provide new insights into digestive physiology and the pathobiology of diarrheal diseases, and will provide new approaches to treat diarrheal diseases. We propose to study parallel aspects of EGF stimulation and carbachol inhibition of BB Na/H exchange. The approaches will involve measuring active Na and C1 transport in ileal mucosal sheets measured with the Ussing chamber/voltage clamp technique, ilea BB vesicle Na/H exchange, and Na/H exchange in the colon cancer cell line Caco-2 stably transfected with NHE3. EGF: a) The mechanism by which PI3-kinase mediates the EGF increase in Na/H exchange will be examined by cell surface biotinylation to determine if the Vmax regulation is due to more molecules of NHE3 on the Caco-2 cell BB or change in NHE3 turnover number and which aspect is dependent on PI3-kinase. Constitutively active PI 3-kinase will allow testing of whether PI 3-kinase activation is sufficient to stimulate BB NHE3. b) The involvement of Src family tyr kinases in stimulation of BB NHE3 will be determined by biochemical studies and use of constitutively active Src family mutants in Caco-2/NHE3 cells. c) The role of the NHE3 C-terminus in its stimulation by EGF when expressed in Caco-2/NHE3 cells will be examined and compared with the formation of signaling complexes with the NHE3 C-terminus partially truncated. Carbachol/protein kinase C: a) The involvement of Src family tyr kinases in inhibition of BB NHE3 by carbachol will be determined by biochemical transport studies in ileum. b) Caco-2/NHE3 cells as a model of carbachol inhibition of NHE3 will be developed. c) The role of the NHE3 C-terminus in inhibition by carbachol/protein kinase C when expressed in Caco-2/NHE3 cells will be examined with C-terminal truncation mutations and point mutations with correlation of formation of signaling complexes and inhibition of NHE3.

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- **Project Title: EAE GENE CLUSTER OF ENTEROPATHOGENIC E COLI**

  Principal Investigator & Institution: Donnenberg, Michael S.; Medicine; University of Maryland Balt Prof School Baltimore, Md 21201

  Timing: Fiscal Year 2001; Project Start 01-FEB-1992; Project End 31-MAR-2002

  Summary: (Adapted from the applicants abstract): Enteropathogenic Escherichia coli (EPEC), a leading cause of infant **diarrhea** worldwide, can attach intimately to host cells, efface microvilli and disrupt the cytoskeleton in a process known as attaching and effacing. A complete characterization of the attaching and effacing effect would greatly advance our understanding of pathogen-host interactions and is the long term goal of this project. The eae gene cluster is required for attaching and effacing. Within this cluster are genes encoding at least two proteins that are secreted by EPEC, EspA and EspB. When expressed in host cells, EspB causes dramatic changes in cellular morphology. In the studies described in this proposal, the proteins encoded by the eae gene cluster will be used as tools to dissect the molecular and cellular events that occur during attaching and effacing. Each of the remaining genes of the cluster will be

mutated to assign a role for each locus in attaching and effacing. Experiments to elucidate functional roles as chaperones, components of the secretion apparatus, and signaling proteins are described. Detailed studies of the precise role of EspB in pathogenesis will be performed to test the primary hypothesis that EspB acts inside the host cell to directly alter signaling proteins involved in cytoskeletal dynamics. The functions of different domains of the EspB protein will be explored in carefully planned structure-function studies. Finally, the role of the EspA protein in pathogenesis will be studied, exploring the hypothesis that EspA is required for EspB translocation to the cell cytoplasm. A detailed understanding of the molecular events that result in the attaching and effacing effect is likely to emerge from these studies. Knowledge of the precise events involved in attaching and effacing will lead to a better understanding of EPEC infection, of enterohemorrhagic E. coli infection, of interactions between bacteria and host cells, and of regulation of the host cell cytoskeleton. This information may result in new strategies for preventing and ameliorating infections.

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

- **Project Title: EHEC INTERACTIONS WITH THE NORMAL INTESTINAL FLORA**

  Principal Investigator & Institution: Sperandio, Vanessa; Microbiology; University of Texas Sw Med Ctr/Dallas Dallas, Tx 753909105

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

  Summary: (provided by applicant): Enterohemorrhagic E. coli (EHEC) O157:H7 is responsible for major outbreaks of bloody **diarrhea** and hemolytic uremic syndrome (HUS) throughout the world. One of the major problems in the control and prevention of EHEC outbreaks is the fact that it has a very low infectious dose. EHEC colonizes the large intestine where it causes attaching and effacing (AE) lesions, which are believed to be the first step toward infection of the host, and also produces Shiga toxins (Stx), which are responsible for the major symptoms of HUS. The genes involved in the formation of these AE lesions are encoded within a chromosomal pathogenicity island named the Locus of Enterocyte Effacement (LEE). We recently reported that both the LEE and the genes encoding Stx are activated by a bacterial cell-to-cell signaling mechanism known as quorum sensing (QS). Bacteria secrete hormone-like compounds, called autoinducers, which interact with bacterial transcriptional regulators to drive gene expression. The QS mechanism employed in this activation is involved in bacterial inter-species communication, and we propose that activation of EHEC virulence genes by this system may occur in response to autoinducers produced by the normal intestinal flora. This could, in part explain the low infectious dose of EHEC. This grant application in response to RFA (AI-02-008) "Impact of microbial interactions on infections diseases" intends to study EHEC virulence gene expression in response to signals produced by the normal intestinal flora. Given that this RFA (AI-02-008) is designed to investigate the impact of microbial interactions on infectious diseases, including the interactions between pathogens and the normal flora, we feel that this grant application is particularly well suited to the mission of the RFA. In Specific Aim 1, we propose to study EHEC gene expression at the genome level using DNA microarrays to assess EHEC responses to signals produced by the normal intestinal flora. In Specific Aim 2, we propose to monitor EHEC virulence gene expression in a mixed population in the presence of the intestinal flora.

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

- **Project Title: ENCEPHALITOZOAN CUNICULI--HOST IMMUNITY AND PATHOGENESIS**

  Principal Investigator & Institution: Khan, Imtiaz A.; Associate Professor; Microbiol/Immunolgy/Parasitlgy; Louisiana State Univ Hsc New Orleans New Orleans, La 70112

  Timing: Fiscal Year 2001; Project Start 15-SEP-1998; Project End 31-AUG-2004

  Summary: Microsporidia are obligate intracellular protozoan parasites which cause wide variety of opportunistic infections in AIDS patients. The most common microsporidium associated with AIDS, Enterocytozoon beneusi, causes chronic **diarrhea** in the HIV-infected individuals. However, an animal model for E. beneusi is not available at present. Most of the experimental studies on microsporidia have been carried out on with Encephalitozoon cuniculi. This microsporidium, which commonly infects rodents, has been reported in humans as well. Several reports of disseminated E. cuniculi infection in HIV-infected patients have appeared recently. E. cuniculi is also very closely related to other microsporidia like Encephalitozoon hellum and Encephalitozoon intestinalis, which are also known to cause complications in AIDS individuals. Very little is known about the immune mechanisms against microsporidial infection in the normal host. The cellular immunity appears to be important for protection against an E. cuniculi challenge. Preliminary studies suggest that CD8+ T cells are an essential component of the immune response. Therefore, the detailed analysis of CD8+ T cell immunity is essential for understanding the immunoprotective mechanism against E. cuniculi infection. The first specific aim in this project will be to evaluate the kinetics of CD8+ T cell response during the course of E. cuniculi infection. The difference in this response between the resistant and susceptible species of mice will be determined and compared; the cytotoxic activity of the CD8+ T cells from the infected normal and immunocompromised animals will be assayed. The second specific aim is to determine the efficacy of the adoptive transfer of immune CD8+ T cells into infected immunocompromise host. Next, the length of time for which the immune CD8+ T cells can retain their activated/memory state in the naive immunocompromised host will be determined. In the third specific aim the role of gamma/delta T cells and the CD4+ T cells in the induction and maintenance of CD8+ T cell immunity will be evaluated. These studies will enable extrapolation to the immune mechanisms against other microsporidia, like E. beneusi, which is more frequently encountered by AIDS patients.

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

- **Project Title: ENCEPHALITOZOON INTESTINALIS SPORE ADHERENCE TO HOST**

  Principal Investigator & Institution: Hayman, James R.; Microbiology; East Tennessee State University Box 70565 Johnson City, Tn 37601

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

  Summary: (provided by applicant): Microsporidia are obligate intracellular opportunistic protozoan pathogens that infect a wide range of vertebrates and invertebrates Although microsporidia have been known to cause disease in animals for more than 150 years, it was in conjunction with the AIDS epidemic that microsporidia were discovered as one of the causes of severe **diarrhea** in some HIV infected individuals The two most common causes of microsporidiosis in humans are Enterocytozoon bieneusi and Encephalitozoon intestinalis Because there is no established method for long term in vitro culture of E bieneusi, E intestinalis is used for

these proposed studies When E intestinalis spores are placed in culture with host cells, the spores adhere to the host cell surfaces Although this adherence occurs seemingly spontaneously and can be viewed by light microscopy, it has not been described Preliminary studies show that E intestinalis spore adherence is specific and can be inhibited by the addition of exogenous glycosaminoglycans or short oligo peptides that contain an RGD (arg-gly-asp) cell attachment motif, indicating that spore adherence may be mediated by two different mechanisms While the optimal conditions for spore germination are not known, it seems logical that spore adherence may be a critical step in the infection process Thus, the overall objective of this research proposal is to characterize the adherence of E intestinalis spores to mammalian host cells and to determine the importance of adherence in the process of infection. The Specific Aims which address the overall objective include (1) determining the mechanism(s) of E intestinalis spore adherence, and (2) clarifying the association of E intestinalis spore adherence and infectivity The results of these proposed studies will aid in elucidation of the biological significance of spore adherence as it relates to infectivity Understanding the mechanism of adherence could lead to the development of novel therapeutic interventions and to the prevention of infection and/or reinfection.

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

- **Project Title: ENDOTHELIAL CELLS, VWF CLEAVAGE, AND THROMBOTIC MICROANGIOPATHIES**

  Principal Investigator & Institution: Moake, Joel L.; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2001; Project Start 06-JUN-2001; Project End 31-JAN-2006

  Summary: At elevated levels of fluid shear stress in vitro, platelet aggregation occurs directly without a requirement for preceding platelet-surface adhesion. This high shear stress-induced platelet aggregation is mediated by the binding of large of large and usually large (UL) von Willebrand factor (vWF) multimers to the platelet surface glycoprotein (GP) complexes, GPIbalpha-IX-V and GPIIb-IIIalpha (aIIb/b3) in the presence of adenosine diphosphate (ADP). In vivo, high shear stress-induced microvascular aggregation mediated by large vWF/ULvWf multimers is the probably cause of systemic platelet aggregation in thrombotic thrombocytopenic purpura (TTP), the most extensive and threatening of all human platelet clumping disorders. The failure to cleave proteolytically large/ULvWf multimers, via a vWF metalloproteinase is the underlying critical defect in most types of TTP. Current techniques for measuring vWF metalloproteinase interaction with large/ULvWf multimers, which is unknown, is the subject of Specific Aim A. In Aim A, we will determine the effects of shear stress on the cleavage of large vWF/unusually large ((UL) vWF multimers by vWF metalloproteinase and, specifically, whether or not surface membranes (endothelial cells, platelets) are required for the enzyme-substrate reaction to proceed. The hemolytic-uremic syndrome (HUS) and bone marrow transplantation (BMT)/chemotherapy-related thrombotic microangiopathy share some clinical characteristics with TTP. In contrast to most types of TTP, the vWF metalloproteinase activity (measured by currently available fluid phase assays) is normal in diarrhea-associated HUS and BMT/chemotherapy-related thrombotic microangiopathy. Nevertheless, plasma vWF multimeric abnormalities in some patients with these disorders suggest that platelet aggregation in renal and other areas of the high shear arterial circulation may be vWF-mediated. We will determine whether or not this it so in Specific Aim B. Although the majority of patients with the various types of TTP are treated effectively by plasma infusion/exchange, may continue to die or suffer crippling cardiovascular complications because they are refractory to

plasma manipulation. Furthermore, no therapy is to die or suffer crippling cardiovascular complications because they are refractory to plasma manipulation. Furthermore, no therapy is consistently effective in HUS or BMT/chemotherapy-related thrombotic microangiopathy. Development of additional therapeutic options is needed urgently, and steps in the direction are the goals of Specific Aim C. Specifically, we will evaluate agents ex vivo that inhibit events in shear-induced, vWF- mediated platelet aggregation, and we will devise a simple purification procedure for vWF metalloproteinase. In several portions of this project, there is important experimental collaboration with Drs. Lopez (SCOR PI) and Project 1), Dong (Core B), Kroll (Project 2), Bray (Project 3) and Thiagarajan (Project 5).

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- **Project Title: ENVIRONMENTAL CHANGE AND DIARRHEAL DISEASE**

  Principal Investigator & Institution: Eisenberg, Joseph Ns.; Environmental Health Sciences; University of California Berkeley Berkeley, Ca 94720

  Timing: Fiscal Year 2003; Project Start 15-JAN-2003; Project End 31-DEC-2007

  Summary: (provided by applicant): Diarrheal diseases are predictable outcomes when fecal-oral pathogens meet human poverty and-dislocation. Are diarrheal diseases sensitive indicators of change in socioeconomic level, resource availability, and human social contacts? Processes like these are extremely difficult to study in a controlled fashion. The construction of a new road in coastal Ecuador provides a valuable natural experiment for this purpose. This road will link some previously remote villages to local, regional, and national networks of goods, services, and people, creating new connections among them. We hypothesize that: (1) the level and type of connections between villages are correlated with infection of enteric pathogens; and (2) the changing social connections, new resources, and sanitary and hygienic behaviors of individuals within villages are correlated with infection of enteric pathogens. These hypotheses use the village as their unit of analysis. When estimating the contribution of various exposure risks to disease incidence, it is also important to explore the implications of interdependence between these pathways. This is the third aim of our study: analyzing the joint effects of changes in these contact patterns using disease transmission models. Using a quasi-experimental design, twenty villages will be followed for 4 years, selected so that a rural-urban continuum is fully represented. This continuum will be measured by several factors that relate a given village to Borbon, the town located at the confluence of two rivers that support the villages within the region. Data will be collected at three levels. First, health promoters who live in the villages under study will implement an active surveillance program. They will administer a new survey tool to measure the incidence of all the diarrheal illnesses and monitor both proximal and distal determinants of disease, in a given village. Second, a biannual visit to each community will be conducted by our field team, which has recently completed a cross sectional feasibility study in these villages. Each visit will last two weeks. In these visits, stool samples will be collected from all symptomatic individuals and a random selection of controls. In addition, during these visits, survey tools will be used to collect information on water-use behavior sanitation, hygiene, food consumption patterns, and travel and migration. Third, semi-annual visits to each village will be undertaken by the local Ecuadorian anthropologist. These visits will include open-ended interviews as well as additional questions about social network formation and change. The visits will also allow village development and road.

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- **Project Title: EPIDEIOLOGY OF SHIGELLOSIS IN THE PERUVIAN AMAZON**

  Principal Investigator & Institution: Kosek, Margaret N.; International Health; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2001; Project Start 25-SEP-2001; Project End 31-JUL-2004

  Summary: (provided by applicant): Shigellosis is the principal cause of clinical dysentery and a frequent cause of morbidity and mortality in children living in impoverished areas. Due to rapid appearance and spread of multiply antibiotic resistant strains and the lack of an available vaccine the morbidity and mortality from shigellosis is likely to increase without improved disease control measures. The proposed study will l) determine the community incidence rates of shigellosis and risk factors for the development of shigellosis in children under six years of age in the Peruvian Amazon; 2) characterize the relative importance of different routes of transmission by the genotyping of isolates from patients, family members, and household environmental sources; and 3) determine the diversity of isolates obtained in households of children with shigellosis and control households by genomic analysis, serotype, and antibiotic sensitivity profile. These data will contribute to an improved understanding of the epidemiology of shigellosis in an endemic area and therefore serve as the basis for the definition of the most highly effective interventions. The information on the serotypic diversity in the population as a whole and in households with children with dysentery will provide important data useful in vaccine development and establish this as a candidate site for future vaccine trials. The development and evaluation of a rapid highly discriminatory molecular typing system that is more readily applicable in less developed regions will facilitate future investigation in endemic areas. The collaborative team that is brought together to conduct the proposed study is an established international group of microbiologists, molecular geneticists, epidemiologists, and physicians with extensive experience training junior scientists in an international setting. This project will further strengthen these international connections in the process of the training of a junior clinician-scientist.

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- **Project Title: EPIDEMIOLOGY AND MECHANISMS OF FECAL INCONTINENCE**

  Principal Investigator & Institution: Bharucha, Adil E.; Mayo Clinic Rochester 200 1St St Sw Rochester, Mn 55905

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

  Summary: Fecal incontinence (FI) is a socially devastating symptom in older women and may contribute to institutionalization. The epidemiology and pathophysiology of "idiopathic" FI is incompletely understood. Current concepts based on tertiary-care studies heavily emphasize the role of anal sphincter defects visualized by endoanal ultrasound. Preliminary studies suggest that the prevalence of FI in Olmsted County in women greater than or equal to 50 years is 17.8 percent with a median age of onset of 61 years. Obstetric events, diarrhea/urgency and obesity are risk factors for FI. Our novel "fluoroscopic" single-shot fast spin-echo MRI techniques visualize pelvic floor descent during defecation in real-time. In contrast to US, endoanal MRI depicts external sphincter defects and atrophy, puborectalis thinning and global pelvic floor laxity. The hypothesis is that fecal incontinence is not attributable to obstetric trauma alone, but the cumulative result of pelvic floor weakness caused by obstetric trauma, excessive straining, obesity, aging and menopause, compounded by **diarrhea.** This hypothesis will be addressed by combining the data infrastructure of the Rochester Epidemiology Project with state- of-the-art physiological measurements in a community-based sample.

A questionnaire will be mailed to a cohort of approximately 1,000 women surveyed previously to ascertain the incidence and natural history of FI, and, a new sample of 5,000 women to determine the prevalence and frequency of FI. Putative risk factors for pelvic floor injury (obstetric trauma, chronic straining, obesity and estrogen depletion) and FI (diarrhea and rectal urgency) will be evaluated in a case-control study of approximately 200 patients with FI at least once a month and approximately 200 controls. approximately 100 patients with FI and approximately 100 controls will have MRI fluoroscopy to characterize the specific global pelvic floor abnormality (i.e., anal sphincter defects, sphincter atrophy, puborectalis thinning and pelvic floor laxity) associated with FI. These studies will refine our understanding of the epidemiology of FI, identify the obstetric risk factors responsible for delayed manifestations of pelvic floor injury, i.e. FI, underscore the importance of non- obstetric risk factors for FI and provide novel insights into the specific pattern of pelvic floor injury associated with FI in a community. These steps are necessary for reducing the incidence of pelvic floor damage by risk factor modification, identifying patients at higher risk of progressing to symptomatic FI, and designing appropriate interventions to halt this process.

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- **Project Title: EPITHELIAL GENE TRANSCRIPTION IN INTESTINAL PATHOLOGY**

  Principal Investigator & Institution: Wu, Gary D.; Associate Professor of Medicine; Medicine; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2001; Project Start 01-AUG-1999; Project End 31-JUL-2003

  Summary: The intestinal epithelium is spatially segregated into a proliferating, undifferentiated compartment and a non- proliferating, differentiated compartment in both the small and large intestine. The differentiated columnar epithelium is the interface between the contents of the intestinal lumen and the internal environment of higher vertebrates and, therefore, expresses genes important for the functional activity at this interface. To date, however, little is known about the following: 1) The molecular mechanism by which genes are targeted to the colonic epithelium, 2) The processes underlying differentiation in the colonic epithelium, or 3) The mechanisms by which intestinal gene regulation is altered in pathologic disease states. Therefore, based upon the following hypothesis, we propose to study the transcriptional regulation of a gene known as DRA (Down Regulated in Adenoma): 1) The regulation of DRA gene expression may be used as a model to understand how gene expression is directed to the differentiated surface epithelium of the colon. DRA encodes a sulfate/chloride anion transporter that is expressed principally by the differentiated epithelium in the colon and whose expression is lost in colonic adenomas and adenocarcinomas. DRA has been recently identified by positional cloning as the gene which is mutated in congenital chloride **diarrhea** and represents the only gene yet identified that, in isolation, plays a role in the pathogenesis of **diarrhea.** We have demonstrated that two zinc finger transcription factors, YY1 and GATA, play an important role in the transcriptional activation of the DRA promoter in vitro. Transgenic animals demonstrate that 3.6 kb of the DRA 5'-flank directs high level reporter gene expression to the differentiated epithelium of both the small and large intestine. Three specific aims will be pursued to understand how the DRA gene is regulated: 1) To elucidate the transcriptional mechanisms by which the DRA 5'-flank is activated using sodium butyrate induction of DRA in LS174T cells as an in vitro model system, 2) To identify potential cis-acting regions within the DRA promoter which interact which nuclear proteins isolated from murine small and large intestine, and 3) To characterize the mechanisms that regulate

DRA gene expression in vivo using transgenic mice. Ultimately, once the mechanisms by which DRA gene transcription is regulated in the normal colon have been elucidated, DRA may be a useful model with which to investigate how gene expression is altered in pathobiology.

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- **Project Title: EPITHELIAL SECRETORY MECHANISMS IN ENTERIC INFECTION**

  Principal Investigator & Institution: Barrett, Kim E.; Professor and Vice Chair for Research; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, Ca 92093

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

  Summary: The long-term goal of the investigator is to improve the understanding and treatment of diarrheal diseases associated with enteric infections. In the context of the Program Project, the goal of the studies proposed in this unit is to provide a functional correlate for host-pathogen interactions defined by other participating investigators. The studies proposed here will focus on two clinically-important enteric pathogens, Salmonella and Giardia, as prototypes of invasive and luminal pathogens, respectively. The overall hypothesis to be tested is that diarrheal illness resulting from infections with these pathogens reflects specific dysfunction of epithelial secretory, absorptive and/or barrier functions, mediated via both direct effects on the epithelium as well as via secondary cell types and mediators. Further, these effects are proposed to involve alterations in either the expression, localization and/or function of key transport and regulatory proteins in the epithelial cells. All studies will be conducted using human-derived model systems given that substantial species differences are known to exist in the development of diarrheal illness in response to infection. Studies will be performed using both reductionist cell line models as well as in xenografts of human intestinal tissue maintained in SCID mice. These latter xenografts, which develop the mature characteristics of pediatric intestine, allow parameters of epithelial function to be assessed in an integrated system. Thus, contributions of non-epithelial cell types to pathology induced by infection can be assessed. They will also allow the study of small intestinal functions, for which adequate cell line models do not exist. Four specific aims are proposed. We will study the effect of infection and pathogenetic mechanisms of changes in (1) chloride secretion, (2) sodium-coupled glucose absorption, (3) brush border disaccharide hydrolysis, and (4) barrier function to small and macro-molecules. The studies will encompass electrophysiological, biochemical and molecular approaches and will be facilitated by the availability of various mutant strains of salmonella. In total, the studies should define paradigms for pathogen-induced intestinal dysfunction. The findings from these studies are accordingly expected to have both basic and clinical implications for our understanding of the intestinal epithelium.

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- **Project Title: ESCHERICHIA COLI STABLE TOXIN**

  Principal Investigator & Institution: Newburg, David S.; Eastern Virginia Medical School Norfolk, Va 23507

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

  Summary: Heat-stable toxin (ST) produce by enterotoxigenic E. coli is a common cause of secretory **diarrhea** among children (in whom it can be fatal) and travels in areas where this pathogen is endemic. In mice, ST-induced **diarrhea** is prevented by ingestion of human milk. This protective activity has been localized to human milk

fucosylooligosaccharides that have alpha 1, 2 linkages at their reducing ends. The amount of alpha 1, 2-linked to other fucosylooligosaccharides in mothers' milk is inversely related to the incidence of ST-associated **diarrhea** in their breastfeeding infants. We conclude that 2-linked fucosyl moieties are critical determinants in protection against ST, probably working in concert with 3- and 4-linked moieties. The fucosyltransferases that synthesize these fucosylooligosaccharides are thought to be expressed by genes of the secretor and Lewis family. We will synthesize a complete combinatorial library of fucosylated tri- and tetrasccharides encompassing the possible products of human milk fucosyltransferases. And then test their ability individually and in combinations, to inhibit ST-induced **diarrhea** in suckling mice. The activities of the most promising compounds will be compared with that of the fucosyloligosaccharide fraction of human milk. The mechanism of inhibition will be studied in cultured human enterocytes. The genetics basis for different levels of protective oligosaccharide in milk from different individuals will be studied. This project will identify fucose. The project will identify fucose-containing structures that inhibit ST, their relative efficacies, and their mechanisms of action. The genetic basis for the expression of fucosylooligosaccharides in milk will be determined. The relationship between their presence in milk and risk of ST **diarrhea** in infants will be investigated. The long-range goals are to develop strategies for determining which infants are at highest risk of this often deadly disease and produce novel, therapeutic fucosylooligosaccharides as a complement for infants at risk.

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- **Project Title: EVALUATION OF ROTAVIRUS VACCINES IN A PRIMATE MODEL**

  Principal Investigator & Institution: Choi, Anthony H.; Emerging Concepts, Inc. 3130 Highland Ave, Ste 3115 Cincinnati, Oh 45219

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

  Summary: (provided by applicant): Rotavirus causes severe **diarrhea** in infants resulting in approximately 600,000 deaths worldwide and costing the United States 1.5 billion dollars annually. The only FDA-approved rotavirus vaccine was withdrawn in 1999 because of its association with intussusception. The subunit rotavirus vaccines that we are developing have been evaluated in a mouse model that measures rotavirus shedding as the endpoint for quantifying vaccine efficacies. Mucosal delivery of the vaccines has been found to elicit nearly complete protection against a subsequent oral rotavirus challenge. Because mice and humans are phylogenetically distant, it is necessary to establish a non-human primate model which will be used to validate the efficacy of our vaccine candidates using reduction of illness as the endpoint for measuring vaccine efficacies. In this proposal, the feasibility of a primate model for evaluating rotavirus vaccines is assessed by determining (1) the size of the "window", in which young rhesus macaques are susceptible to developing **diarrhea** following rotavirus-induced illness and (3) whether titers of rotavirus-specific antibodies, and upregulated levels of cytokines in effector CD4+ and CD8+ lymphocytes correlate with protection. In a follow-up SBIR application, we will scale up and produce GMP-quality vaccines which will be used in safety and immunogenicity trials.

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- **Project Title: FUNCTION OF PLATELETS AND COAGULATION FACTORS**

  Principal Investigator & Institution: Majerus, Philip W.; Professor; Internal Medicine; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

Timing: Fiscal Year 2001; Project Start 01-APR-1979; Project End 31-MAR-2004

Summary: (Adapted from the Applicant's Abstract) This grant has as its goal the elucidation of the mechanisms by which the phosphatidylinositol signalling system evokes intracellular responses to extracellular agonists. Understanding this system will provide new insights into platelet physiology and pathology and also into the proliferation and differentiation of megakaryocytes. The experiements will also address the pathogenesis of several disease states in which defects in inositol signalling are present. In particular, the applicant will study the relationship between inositol polyphosphate 4-phosphatase (4-Ptase) and phosphatidylinositol 3-kinase in platelets. He will investigate the mechanism by which 4-Ptase controls megakaryocyte proliferation in GATA-1 null megakaryocytes. In the absence of 4-Ptase, these megakaryocytes proliferate continuously and fail to produce platelets. Restoration of 4-Ptase arrests megakaryocyte growth. He will use NIH 3T3 cells to investigate whether this growth arresting property of 4-Ptase is general. He will investigate the homolog of 4-Ptase, SopB, a Salmonella gene required for virulence. In the absence of SopB, the organisms infect intestinal epithelia but fail to induce neutrophilic infiltration and **diarrhea.** SopB is an inositol phosphatase and enzyme activity is required for virulence. The substrate specificity and derangement of inositol metabolism in infected cells will be determined. He will study another homolog of 4-Ptase that is a tumor suppressor gene (PTEN) and is also an inositol phosphatase. The OCRL-1 5-phosphatase that when mutated is the cause of Lowe Syndrome will be examined. The applicant propose that the defect results in abnormal targeting of lysosomal enzyme in Lowe Syndrome. He plans to study this and to measure plasma lysosomal enzymes in patients with Lowe Syndrome. He will also attempt to elucidate the enzymology and regulation of production of isomers of inositol tetraphosphates and inositol pentaphosphates. He will identify, isolate, and clone cDNA for enzymes leading to InsP5 starting with inositol 1,3,4-triphosphate 5/6-kinase.

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- **Project Title: FUNCTION OF THE ENTERIC NERVOUS SYSTEM**

  Principal Investigator & Institution: Wood, Jackie D.; Professor and Chairman; Physiology and Cell Biology; Ohio State University 1800 Cannon Dr, Rm 1210 Columbus, Oh 43210

  Timing: Fiscal Year 2001; Project Start 01-SEP-1985; Project End 31-MAR-2002

  Summary: This is a renewal application that will use neurophysiologic methods of electrophysiologic recording to test the general hypothesis that signaling interactions occur between the immune system and nervous system of the gastrointestinal tract. The current proposal focuses mainly on the mast cell component of the immunologic cell population and tests the hypothesis that mast cells function to signal the presence of specific allergens to the enteric nervous system. The enteric nervous system responds in a specific way by calling-up a specialized behavioral program stored in its microcircuits which leads to a stereotypic pattern of intestinal behavior of copious secretion of water, mucous and electrolytes in coordination with a powerful propulsive motility pattern. This response pattern functions to expel allergens from the lumen with accompanying symptoms of **diarrhea** and abdominal pain. Aim 1 will identify the actions on enteric neurons of histamine released by intestinal mast cells during allergen-induced degranulation in the myenteric and submucous plexuses of the small and large intestine and the myenteric plexus of the stomach. Aim 2 will determine the morphological and immunohistochemical types of enteric neurons on which specific effects of allergen-induced release of histamine occur. Aims 3 and 4 will determine how inflammatory

cytokines affect morphologically identified enteric neurons using approaches similar to those in aims 1 and 2. Aim 5 is to identify how enteric neural networks interact and respond to signals from immune cells. Aim 6 will determine how the enterotoxin of Clostridium difficile acts on the intestinal nervous system to evoke neurogenic inflammation. The overall goal of the study is to understand better the neurophysiology underlying gastrointestinal immuno-neural communication and its involvement in the symptomatology of **diarrhea,** abdominal pain and intestinal inflammation.

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- **Project Title: FUNCTIONAL BOWEL DISORDERS IN CHINESE MEDICINE**

  Principal Investigator & Institution: Berman, Brian M.; Director; Family Medicine; University of Maryland Balt Prof School Baltimore, Md 21201

  Timing: Fiscal Year 2003; Project Start 22-SEP-2003; Project End 31-MAR-2005

  Summary: (provided by applicant): This application is for a Planning Grant for International Centers for Research on Complementary and Alternative Medicine (PICRC) in response to RFA AT-03-002. The goal of planning phase activities is to begin creation of the Functional Bowel Disorders and Traditional Chinese Medicine Research Group, with the participation of consortium members of three universities, The University of Maryland Center for Integrative Medicine, the Chinese University of Hong Kong, and the University of Illinois at Chicago Program for Collaborative Research in the Pharmaceutical Sciences. The consortium will develop a grant application for an International Center for Research on Complementary and Alternative Medicine (ICRC) to be submitted during the two-year planning phase, which will request funding to support three pilot projects related to irritable bowel syndrome and three cores: a Pharmacologic Core, a Data Management, Analysis, and Coordination Core, and an Administrative Core. The projects to be proposed will include 1) a rat model irritable bowel syndrome treatment trial using acupuncture and herbs, 2) a human pathophysiology pilot study on the effect of TCM on cerebral cortical activation and visceral sensation to rectal distension in IBS patients and non-IBS volunteers, and 3) Phase I and II clinical trials of TCM treatment in diarrhea-type IBS patients. Pilot studies in the animal model, standardization and authentication of the herbal preparation, and the techniques of human rectal distension in the functional MRI environment will be conducted in the planning phase to facilitate the projects to be proposed.

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- **Project Title: GENE POLYMORPHISMS PREDISPOSING TO INFECTIOUS DIARRHEA**

  Principal Investigator & Institution: Okhuysen, Pablo C.; Associate Professor; Internal Medicine; University of Texas Hlth Sci Ctr Houston Box 20036 Houston, Tx 77225

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-DEC-2007

  Summary: (provided by applicant): After exposure to an enteropathogen, the manifestations of infectious **diarrhea** are variable and depend on host and pathogen factors. A variety of host factors modulate the likelihood of infection or severity of symptoms and can be categorized as those that mediate susceptibility (i.e., host genetic factors, pathogen receptors), and injury (i.e., stimulation of fluid and electrolyte channels, pro inflammatory cytokines). Resolution of infection is determined by factors that contribute to the phases of control and healing (i.e., anti-inflammatory cytokines and specific immunity). Our central hypothesis is that genetic polymorphisms that lead to qualitative or quantitative differences in one or several of these mediators are

partially responsible for the development of infection and illness after exposure to enteric pathogens. To this end we will study two well-characterized populations of subjects with infectious **diarrhea.** The first study group will consist of healthy adults traveling from developed nations to areas of risk for infection with bacterial agents of **diarrhea.** The second study group will consist of healthy adults experimentally exposed to Cryptosporidium at the University of Texas - Houston Clinical Research Center. For both we propose to investigate host single nucleotide polymorphisms (SNPs) of genes that encode proteins that are associated with either susceptibility, modulation of disease manifestation (injury), eradication (control) and healing after infection. We will focus on three agents with potential for bioterrorism use by waterborne or food borne routes with distinct pathophysiology; enterotoxigenic E. coli a cause of secretory **diarrhea,** Enteroaggregative E. coli, a cause of inflammatory **diarrhea** and Cryptosporidium an intracellular pathogen. SNPs will be correlated with the isolation of an enteropathogen and clinical illness. The impact of SNPs will be examined in the context of different ethnic backgrounds. The understanding of the outcome of infection as they relate to host genetic factors will be of use in designing biodefense interventions that are directed towards improving risk assessment. The identification of populations that are more susceptible or vulnerable to the effects of enteric pathogens will be important in the design of strategies to decrease the impact that these agents may have in causing disease and defining the populations most likely to benefit from prevention, treatment and or vaccines.

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- **Project Title: GENETIC ANALYSIS OF CHOLERA TOXIN STRUCTURE AND FUNCTION**

  Principal Investigator & Institution: Holmes, Randall K.; Professor and Chair; Microbiology; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

  Timing: Fiscal Year 2002; Project Start 01-FEB-1992; Project End 31-JAN-2007

  Summary: (Adapted from the Applicant's Abstract): Approximately 1.5 billion cases of **diarrhea** cause 4 million deaths annually in children under 5 years old, and 5-7 million cases of cholera cause about100,000 deaths. Cholera toxin (CT) from Vibrio cholerae causes the massive watery **diarrhea** of cholera. Enterotoxigenic E. coli (ETEC) cause up to 20 percent of diarrheal disease in developing countries, and produce heat-labile enterotoxins called LTI and LTII that are closely related to CT in structure and function. The best current vaccines against cholera provide only moderate protection for short periods of time and are not licensed in the United States, and there are no vaccines for human use against ETEC. CT and related enterotoxins are potent immunogens and mucosal adjuvants, and they are also used widely as tools to investigate the role of heterotrimeric G proteins in signal transduction, the role of gangliosides in endocytosis and vesicular trafficking, the mapping and/or ablation of neural pathways, and many other cell functions. We study the structure and function of CT and use LTI and LTII in comparative studies to explore the molecular basis for functional differences between them. Our long term goals are to elucidate the molecular basis for biological activities of CT and related enterotoxins, and to use that knowledge to design novel structure-based vaccines and therapeutics to prevent or treat enterotoxic diarrheas. CT, LTI or LTII are also being studied widely as vaccine components, adjuvants or immunomodulators to prevent or treat diseases unrelated to enterotoxic diarrheas. Important issues concerning structure and function of CT that are not yet understood include identifying and characterizing: conformational changes that activate the catalytic capacity of CT-A1 after

nicking and reduction of CT holotoxin; motifs on CT-A1 that determine its interactions with Gsalpha/beta/gamma as a substrate for ADP ribosylation and with ADP-ribosylation factors (ARFs) as stimulators of catalytic activity; features of CT-A and CT-B that enable them to assemble spontaneously into CT holotoxin; mechanisms by which binding of enterotoxins to plasma membrane receptors determines their trafficking within target cells; and pathway(s) by which CT-A1 is translocated from the ER to the cytoplasm to reach its intracellular target and cause toxicity. During the next project period we will use a wide variety of novel methods from microbiology, genetics, biochemistry, cell biology and structural biology to investigate these important current issues concerning the structure and function of cholera toxin.

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- **Project Title: GENETIC VARIABILITY OF E. HISTOLYTICA IN TURKEY**

  Principal Investigator & Institution: Petri, William A.; Chief; Internal Medicine; University of Virginia Charlottesville Box 400195 Charlottesville, Va 22904

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

  Summary: (provided by applicant) Amebiasis is a deadly parasitic infectious disease. We propose to re-examine the epidemiology of amebiasis in Turkey using modern diagnostic tests and also test for genetic differences between strains of Entameoba histolytica that cause asymptomatic infection, colitis and liver abscess. In Specific Aim 1, we will determine the prevalence of amebiasis in Van, a city in the east region of Turkey using diagnostic techniques (antigen detection based-ELISA test and amebic-specific PCR) on stool samples of patients with **diarrhea,** dysentery and stool samples from asymptomatic individuals. We hypothesize that E. histolytica is a more frequent cause of **diarrhea** and dysentery in Van than has been determined by stool "ova and parasite" exams. A more accurate estimate of the burden of disease due to amebiasis is important for design of treatment and prevention strategies. After diagnosis of patients with intestinal amebiasis and liver abscess, we will test if genetic differences exist between liver abscess and intestinal isolates of E. histolytica in Specific Aim 2. Genetic diversity will be determined by 1) nested PCR amplification and sequencing of the CRD region of the lectin gene, 2) nested PCR -SREHP gene and 3) DNA microarray analysis. This project will be carried out at the Gulhane Military Medical Academy, Turkey, in collaboration with the University of Virginia. This proposal study is an extension of NIH grant #R01 Al 26649-12.

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- **Project Title: GLYCOSYLATION OF CAMPYLOBACTER FLAGELLA**

  Principal Investigator & Institution: Guerry, Patricia; Section Head; Henry M. Jackson Fdn for the Adv Mil/Med Rockville, Md 20852

  Timing: Fiscal Year 2003; Project Start 01-JUL-1999; Project End 31-MAR-2008

  Summary: (provided by applicant): Campylobacter jejuni is the leading cause of foodborne illness in North America and is among the major causes of bacterial **diarrhea** worldwide. Flagella and motility are required for intestinal colonization and invasion of intestinal epithelial cells by C. jejuni, and flagellin is an immunodominant and possibly a protective antigen. Flagellin from C. jejuni strain 81-176 and Campylobacter coli strain VC167 are glycosylated at 19 and 16 serine or threonine residues, respectively, with a 9 carbon sugar called pseudaminic acid and derivatives of pseudaminic acid. The modifications, which account for approximately 10% of the weight of these glycoproteins, are surface exposed on the flagella filament and are likely involved in

interaction of flagellin with the eukaryotic host. Genetic analyses indicate that the pathway for biosynthesis of pseudaminic acid is conserved in both 81-176 and VC167. Flagellins from both strains contain minor modifications that are acetamidino forms of pseudaminic acid (mass 315 Da). However, the 315 Da group synthesized by 81-176 and VC 167 are structurally and immunologically distinct and are synthesized by independent pathways in each organism. The data suggest that campylobacter flagellin needs to be glycosylated in order to be exported and/or assembled into a filament. A mutant in 81-176 that is unable to synthesize the acetamidino form of pseudaminic acid appears to be attenuated in virulence. The aim of this study is to further elucidate the pathways by which the different forms of pseudaminic acid are synthesized and to study unique aspects of the regulation of these glycosylation genes. Site-specific mutagenesis will be done on flagellin to eliminate modification sites sequentially in order to determine sites that are critical for flagella function and the rules of site occupancy. The biological role of flagella glycosylation will be studied by examining a series of mutants in in vitro and in vivo assays of virulence.

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

- **Project Title: HOST CELL KILLING BY EPEC: CENTRAL ROLE IN PATHOGENESIS**

  Principal Investigator & Institution: Crane, John K.; Medicine; State University of New York at Buffalo Suite 211 Ub Commons Amherst, Ny 14228

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-JAN-2006

  Summary: (provided by applicant): Enteropathogenic E. coli (EPEC) is a common cause of severe, watery **diarrhea** in children in developing countries. EPEC is also the prototype of a group of attaching and effacing intestinal pathogens, including enterohemorrhagic E. coli (EHEC, such as O157:H7), Citrobacter rodentium, Hafnia alvei, and EPEC-like E. coli strains of domestic animals. Unlike many other E. coli strains that cause **diarrhea,** EPEC produces no known toxins, so the way it causes disease has been puzzling. Despite major advances in understanding how EPEC adhere, trigger cytoskeletal rearrangements in the host, and cause other host cell alterations, the mechanism by which EPEC causes **diarrhea** has been unclear. The discovery that EPEC triggers host cell death provided an important lead in how EPEC causes disease. The mode of cell death triggered by EPEC has features of both apoptosis (programmed cell death) and necrosis. One of the non-apoptotic features of EPEC-mediated killing is release of adenosine triphosphate (ATP) from the host cell. Once released, ATP is broken down to other adenine nucleotides and adenosine. Adenosine itself acts as a potent secretatagogue, i.e., a stimulator of intestinal fluid and electrolyte secretion, which may cause or contribute to watery **diarrhea.** The present application seeks to understand how EPEC triggers the ATP release from the host, with a particular focus on the role of the cystic fibrosis transmembrane regulator (CFTR). Other goals include determining the signaling pathways activated by adenosine which activate intestinal secretion, and the determining the extent of release of adenine nucleotides into the intestinal tract of rabbits infected with the EPEC-like pathogens rabbit diarrheagenic E. coli (RDEC-1) and rabbit EPEC (REPEC).

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

- **Project Title: HUMAN INTESTINAL DRA--FUNCTION AND REGULATION**

  Principal Investigator & Institution: Alrefai, Waddah A.; Medicine; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

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

Summary: (provided by applicant): The current proposal is aimed at providing the PI with extensive training in advanced molecular biology along with formal courses at the graduate level to enhance his research and laboratory skills. The experienced sponsor- and co-sponsor, along with a highly interactive basic-research environment at the section of Gastroenterology at the Univ. of IL at Chicago, offer a great training opportunity for the PI to achieve his career goals in becoming an independent basic-research investigator in the area of the physiology of intestinal transport. The proposed studies are aimed at examining the exact role of the DRA (Down Regulated in Adenoma) gene in the intestinal Cl- absorption. The DRA gene was shown to be mutated in patients with Congenital Chloride **Diarrhea** (CLD) disease, where the basic defect is an impaired intestinal apical membrane Cl-/HCO3 exchange process. However, DRA cDNA has a high sequence homology with sulfate transporters. DRA was initially shown to be a sulfate/oxalate transporter. Data from few recent studies also indicated that DRA might function as a Cl- transporter. However, in contrast, our recent studies along with studies from other laboratories provide strong evidence that DRA itself may not encode for the conventional intestinal luminal Cl-/HCO3' exchanger. Therefore, it is critical to investigate the precise functional role of DRA in Cl-transport. In Specific Aim 1, we will examine the role of DRA utilizing the anti-sense technique to attenuate its endogenous expression in Caco2 cells and study its effect on SO4--and Cl- transport processes, along with Structure/Function studies to reveal the mechanism(s) by which DRA mutations affects the intestinal Cl- transport. Specific Aim 2 will focus on the mechanism(s) involved in DRA targeting to the plasma membrane. In Specific Aim 3, we will elucidate the transcriptional regulation of DRA, whereas in Specific Aim 4, we will identify proteins interacting with DRA, and possibly a novel intestinal apical membrane Cl- /HCO3 exchanger by screening human colonic cDNA library utilizing the Yeast Two-Hybrid System. The proposed studies will significantly enhance our understanding of the pathophysiological basis of Congenital Chloride **Diarrhea** and **diarrhea** in other colonic diseases.

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

- **Project Title: IDENTIFICATION OF NOVEL ANTIVIRAL TARGETS USING RNAI**

  Principal Investigator & Institution: Pachuk, Catherine J.; Nucleonics, Inc. 26 Spring Mill Dr Malvern, Pa 19355

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

  Summary: (provided by applicant): The goal of this project is to develop a selection strategy using RNA interference (RNAi) to identify novel therapeutic targets for the treatment of cytolytic virus infection. RNAi is a cellular process that causes targeted elimination (silencing) of mRNA. Nucleonics, Inc. has developed platform technologies to exploit RNAi for development of therapeutics and genomic applications. These technologies provide powerful new tools for targeted elimination of specific mRNAs. RNAi will be used to selectively silence genes required for cytolytic virus replication thereby producing cells that will be resistant to infection. Repeated rounds of selection (infection with cytolytic virus) and enrichment (isolation of RNAi-inducing sequences in surviving cells) will identify genes that are potential therapeutic targets for treatment of virus infection. Phase I of this application focuses on (i) optimizing vectors and delivery systems for inducing RNAi in mammalian cells and (ii) "proof-of-concept" tests using these vectors and delivery systems to silence viral and cellular genes known to be required for cytolytic virus replication. Two cytolytic viruses will be tested in this system, a DNA containing virus, human herpes simplex virus type I (HSV-1), and an

RNA containing virus, bovine viral **diarrhea** virus (BVDV). BVDV is a tissue culture surrogate for hepatitis C virus. Phase II of this proposal focuses on using this selection to identify novel genes required for cytolytic virus infection and validate these novel targets in cell culture and animal models of infection.

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

- **Project Title: IMMUNE RESPONSES DURING MEASLES VIRUS INFECTION**

  Principal Investigator & Institution: Griffin, Diane E.; Professor & Chair; Molecular Microbiol and Immun; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2003; Project Start 01-DEC-1985; Project End 31-DEC-2007

  Summary: (provided by applicant): Measles remains a major cause of morbidity and mortality worldwide due to problems with delivery, acceptance and timing of measles immunization. An additional contributor to the continued failure of measles control may be the epidemic of human immunodeficiency virus (HIV) in developing countries, particularly sub-Saharan Africa, where many of the measles deaths occur. The primary complications of measles are pneumonia, otitis media, **diarrhea** and post-infectious encephalomyelitis and the effect of measles virus (MV) on the immune system is important in the development of these complications. Delayed type hypersensitivity skin test responses, natural killer cell activity and mitogen-induced proliferative responses are depressed and plasma IgE is increased for weeks after infection. At the same time, the immune response is effective in clearing virus from tissue and in establishing lifelong immunity to reinfection. Our studies of measles in the US and Peru have determined: (i) that monocytes, epithelial cells and endothelial cells are the primary sites of MV replication in vivo; (ii) that there is immune system activation during the period of "immune suppression"; and (iii) that type 2 cytokines are the predominant T cell cytokines expressed late in the response to MV. In vitro studies have shown that MV interaction with CD46 suppresses production of IL-12 by macrophages and that MV infection of B cells synergizes with IL-4 to induce IgE class switching. Recent studies in Zambian children have shown that concurrent HIV infection slows clearance of MV, that many children have baseline skewing of cytokine responses toward production of IL-5, and that measles transiently, but profoundly, suppresses HIV replication. To define the role of host immune responses during measles and the effect of concurrent HIV infection on these responses, we propose the fol]owing specific aims: 1. To determine the effects of MV infection on antigen presenting cells in vivo and in vitro and the consequences of these effects for the immune response. 2. To determine the role of CD8 T cells in MV clearance and the effect of concurrent HIV infection on this role. 3. To determine the roles of different CD4 and CD8 T cell populations in production of cytokines at various times during measles and the effect of concurrent HIV infection on these roles.

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

- **Project Title: INTESTINAL CYTOKINES IN CRYPTOSPORIDIOSIS**

  Principal Investigator & Institution: White, Arthur C.; Professor; Medicine; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2001; Project Start 01-SEP-1997; Project End 31-JUL-2006

  Summary: (Provided by the applicant): Cryptosporidium parvum is a major cause of **diarrhea** worldwide, for which there is no reliable antiparasitic therapy. In immunocompetent individuals, C. parvum infection results in a self-limited diarrheal

illness. By contrast, AIDS patients may develop chronic **diarrhea,** which can be fatal. Effective antiretroviral therapy can lead to resolution of AiDS-associated cryptosporidiosis, presumably due to improvement in the intestinal immune response. The long-term goals of this project are to determine the immune mechanisms involved in the control of cryptosporidiosis in healthy adults and AIDS patients on effective antiretroviral treatment. We have demonstrated that sensitized, immunocompetent volunteers expressed interferon gamma (IFNT) in response to C. parvum exposure and that IFN7 expression was associated with resistance to infection. By contrast, naive, symptomatic individuals initially expressed Interleukin 15 (IL-15), which was associated with control of oocyst excretion. Neither IL-15 nor IFN7 was detected in AIDS-associated chronic cryptosporidiosis, but expression of IL-15 and IFN7 was noted in biopsies obtained from patients responding to antiretroviral therapy. Preliminary studies demonstrated that IL-15 can activate lymphocytes to lyse infected epithelial cells. However, many questions remain. For example, what are the effector mechanisms used by IL-15 and IFNgamma, in the control phase and how are these responses coordinated? Can Thl cytokines in fact lead to resolution of cryptosporidiosis in AIDS patients in the absence of immune recovery? What is the sequence of responses in AIDS patients with immune recovery with effective anti-retroviral therapy. The specific aims of the current proposal are: 1) To test the hypothesis that IL-15 and IFNgamma help clear infection of epithelial cells by activation of cytolytic cells and establish the mechanisms used by the effector cells. 2) To confirm the importance of Thl cytokines in resolution of cryptosporidiosis by conducting a pilot, proof-of-concept, open-label trial of IL-12 therapy in chronic cryptosporidiosis in AIDS patients not responding to antiretroviral therapy. 3) To confirm that mechanisms used by cytolytic cells defined in aim 1 and associated cytokines, effector molecules, and chemokines are expressed in the intestines in human cryptosporidiosis using microarray analysis of intestinal biopsies obtained before and after experimental challenge of immunocompetent adults with C. parvurn oocysts. 4) To test the hypothesis that AIDS patients with cryptosporidiosis sequentially expresses innate and then Thl memory responses during immune reconstitution. These studies should identify key aspects of the human immune response needed for vaccines to prevent cryptosporidiosis and identify the host responses that can be targeted for adjunctive immunotherapy for cryptosporidiosis in patients with AIDS and other immunodeficiencies. The results should also provide insights into the mechanisms involved in mucosal immunity to other intracellular pathogens.

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- **Project Title: INTESTINAL DEFENSE & SUSCEPTIBILITY IN VIRAL ENTERITIS**

  Principal Investigator & Institution: Bass, Dorsey M.; Pediatrics; Stanford University Stanford, Ca 94305

  Timing: Fiscal Year 2001; Project Start 15-SEP-1998; Project End 31-JUL-2003

  Summary: This is the resubmission of a new application to study intestinal defense and susceptibility in viral enteritis. The intestinal epithelium must function both as a barrier to noxious agents such as toxins and microorganisms and as a site of absorption for essential nutrients. In viral gastroenteritis, pathogenic viruses damage the barrier function of the gut with resultant failure of absorption of critical nutrients including water and salt. The central objective of this proposal is to better understand factors which determine whether enteric viruses such as astrovirus will succeed in producing infection and disease. Proteolytic enzymes in the intestinal lumen dramatically enhance astrovirus infection. The mechanism by which the astrovirus capsid protein is

preteolytically processed and the nature of the enhanced infectivity will be defined in one series of experiments. Epitopes of astrovirus which elicit protective, neutralizing antibodies will be defined and mapped in vitro using monoclonal antibodies. The mechanisms by which these antibodies neutralize astrovirus will be explored. Systemic and mucosal humoral immune responses in children with astrovirus infection will be characterized and compared to the in vitro neutralizing epitope studies. Astrovirus infection of children in a pediatric hospital will be monitored by active surveillance and correlated with known and suspected risk factors for infection and disease. Viral gastroenteritis is a very important public health problem both in the developed world where **diarrhea** leads to thousands of hospitalizations and in the developing world where hundreds of thousands of children die from diarrheal disease. Studies such as these can lead to better understanding of intestinal barrier function and how it can be overcome. Such understanding may lead to better strategies for treatment and prevention of a variety of intestinal illnesses.

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- **Project Title: INTESTINAL DISEASE: ENTEROCYTE/TOXIN INTERACTION**

  Principal Investigator & Institution: Lencer, Wayne I.; Associate Professor; Children's Hospital (Boston) Boston, Ma 021155737

  Timing: Fiscal Year 2001; Project Start 01-SEP-1993; Project End 31-MAY-2006

  Summary: (Applicant's Abstract): Cholera toxin (CT) produced by Vibrio cholerae is the virulence factor responsible for the massive secretory **diarrhea** seen in Asiatic cholera. To induce disease, CT must bind ganglioside GM1 on the host cell apical membrane, enter the cell by endocytosis, and then somehow cross the cell to activate adenylyl cyclase on the cytoplasmic surface of the basolateral membrane. The investigator published data show that CT may move retrograde through Golgi and ER before arrival at the basolateral membrane, and that sorting into this pathway may depend on the lipid-based membrane anchor provided by the toxin's receptor GM1. GM1 concentrates CT in detergent-insoluble glycolipid-rich apical membrane microdomains (DIGs or "lipid rafts"). The applicant hypothesizes that GM1 endows CT with a lipid-based sorting motif that specifies association with DIGs and trafficking into the apical endosome, Golgi cisternae, ER, or transcytotic pathway. It is also not known how the toxin's enzymatic A-subunit enters the cytosol of host cells. Since CT must enter the ER for bioactivity, the investigator hypothesizes that C2 opportunistically utilizes the ER associated degradation system (ERAD) to unfold and cross the membrane via a protein translocase, possibly sec61p. To test these ideas, the applicant will define whether the ceramide domain of GM1 specifies the selective association with DIGs and toxin action in polarized T84 cells. The PI will use toxin variants deficient in clustering GM1 to test if cross-linking individual gangliosides is a prerequisite for association with DIGs or toxin function. The PI will examine raft dependence on membrane cholesterol by using beta-methyl-cyclodextrin, heterogeneity in GM1 content by using a CT variant attenuated in binding GM1, and functional association with the cortical cytoskeleton by membrane fractionation, disruption of actin filaments, and depletion of cholesterol. To test whether GM1 specifies toxin sorting into Golgi and ER, as opposed to the endosome-lysosomal or direct transcytotic pathway, the intracellular itinerary of CT (that binds GM1) and the closely related E. coli toxin LTIIb (that binds ganglioside GD1a) will be systematically compared. Toxin entry into the Golgi or ER, will be defined by microscopy and by exploiting the trans-Golgi specific transfer of sulfate and the ER specific transfer of N-linked oligosaccharides to label CT in these compartments. The mechanism of toxin-unfolding and dislocation from the ER to cytosol will be examined in vitro using

purified ER lumenal and membrane proteins, and in intact T84 cells through the use of selected toxin variants lacking sites for proteolytic nicking, ubiqitination and the cysl87-199 disulfide bond in the toxin's enzymatic A-subunit.

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- **Project Title: INTESTINAL SECRETION & INFLAMMATION - IMPACT OF AMMONIA**

  Principal Investigator & Institution: Matthews, Jeffrey B.; Christian R. Holmes Professor and Chairm; Surgery; University of Cincinnati 2624 Clifton Ave Cincinnati, Oh 45221

  Timing: Fiscal Year 2001; Project Start 01-SEP-1996; Project End 31-AUG-2005

  Summary: Numerous diseases affecting the GI tract, ranging from secretory **diarrhea** to cystic fibrosis, are characterized by dysregulation of epithelial C1- secretion. This project originally identified that ammonium ion (NH4+, normally present at high concentrations in the colonic lumen) may be a novel endogenous regulator of C1-secretion via effects via effects on K+ channels and begins to define the interaction of NH4+ with the basolateral membrane K+ transporters also required for Cl-secretion. Based on work already accomplished, the current application considers how altered K+ channel regulation may influence various intestinal disease states. Preliminary data indicate that the ammonia-derived oxidant monochloramine (NH2Cl) may contribute to the **diarrhea** of colitis by potentiating Ca2+- dependent K+ channels. Experiments also suggest that docosahexaenoic acid (DHA, a component of fish oil) can augment Ca+2-dependent K+ channels, finding of particular interest as DHA begins clinical evaluation as therapy in CF. Preliminary findings suggest that the actin cytoskeleton an functionally alter Ca2+-dependent K+ channels, and conversely, that these K+ channels can modulate cell functions such as epithelial restitution that involve actin remodeling. Three sets of studies are proposed. First, the impact of ammonia on colonic epithelial transport will be further characterized in cultured epithelial ells and in human colonic mucosal preparations, with attention to the interaction of NH4+ with the basolateral Na+-k+-2Cl- co- transporter, Na+_K+ ATPase, and K+ channels. Second, potentiation of basolateral Ca+2-dependent K+ channels by cAMP and NH2Cl will be explored using cultured epithelial cells as model systems with the goal of defining a common mechanism for K+ channel potentiation by these seemingly diverse stimuli. The potential for therapeutic modulation of basolateral K + channels will be explored, specifically examining wheth4r docosahexaenoic acid (DHA) can augment Ca2+-dependent Cl- secretion in T84 cells and human colon, and, if so, to determine its mechanism of action. Finally, the studies will define the effect of chemical manipulation of F-actin on Ca2+-dependent K+ channel regulation and extend preliminary findings suggesting that K+ channel regulation affects the actin-regulated process of epithelial restitution. These studies highlight the importance of basolateral K+ channels in the regulation of secretion and other epithelial functions and reinforce their potential as targets for new drug design.

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- **Project Title: INVOLVEMENT OF TNF-ALPHA IN INTESTINAL INFLAMMATION IN A MODEL OF COLITIS**

  Principal Investigator & Institution: Appleyard, Caroline B.; Associate Professor; Ponce School of Medicine G.P.O. Box 7004 Ponce, Pr 00731

  Timing: Fiscal Year 2001; Project Start 30-SEP-1986; Project End 31-MAY-2005

Description (provided by applicant): Ailments of the gastrointestinal tract are often very debilitating yet despite decades of research, the basic pathogenic mechanisms involved in inflammatory bowel diseases (IBD) are unknown with no cure for diseases such as Crohn?s and Ulcerative Colitis. Until now the lack of a clinically relevant animal model which mimics the periods of remission and relapse seen in the human condition has limited our understanding of the disease pathogenesis. The recent development of a "reactivated" model of colitis represents a more realistic model for the study of colitis-induced inflammation and ulceration. Previous investigations have shown significantly increased levels of inflammatory mediators in inflammatory bowel disease (IBD). This has led to the suggestion that cytokines, prostaglandins and leukotrienes may play an important role in the pathogenesis of IBD. Recent data suggest that the proinflammatory mediator tumor necrosis factor alpha (TNF-alpha) may be a key player in thc inflammatory process. Three sets of experiments will test this central hypothesis: (1) Absolute levels of TNF-alpha will be measured in a reactivated animal model of colitis and the possible cellular source will be investigated (hypothesis: TNF-alpha levels are increased in periods of relapse and inflammation in inflammatory bowel disease). (2) The underlying mechanism of action of TNF-alpha will be characterized by the administration of various inhibitors, drugs or antibodies (hypothesis: involvement of TNF-alpha in this reactivated model of colitis is an essential step in the inflammatory process and resultant ulceration; moreover this is regulated by the nuclear transcription factor kappa beta, NF-kB). (3) The effect of TNF-alpha on ion transport will be investigated using Ussing chambers (hypothesis: TNF-alpha contributes to the pathogenesis of one of the major symptoms of IBD, diarrhea). This research will advance our understanding of the cytokine network and interactions involved in inflammatory bowel disease. It will provide new avenues for potential therapeutic intervention and, ultimately, offer a preferable alternative to the pharmacologic agents and surgical procedures currently employed.

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- **Project Title: IRINOTECAN IN COMBINATION WITH CELECOXIB**

  Principal Investigator & Institution: Rustum, Youcef M.; Senior Vice President for Scientific Aff; Roswell Park Cancer Institute Corp Buffalo, Ny 14263

  Timing: Fiscal Year 2003; Project Start 22-SEP-2003; Project End 31-AUG-2005

  Summary: (provided by applicant): **Diarrhea** and neutropenia are common and often dose-limiting toxicities associated with clinically active chemotherapeutic agents, including irinotecan, the drug of focus in this proposal. Although irinotecan/FU/LV is considered a standard therapy in the treatment of patients with advanced colorectal cancer, a significant number of treated patients remain clinically resistant and grade Ill/IV **diarrhea** (approximately 30%) and neutropenia (approximately 15%) are common. These toxicities compromise the quality of life of responders and non-responders alike. Thus, there is a critical and pressing need to identify and evaluate approaches that could impact positively on the therapeutic selectivity and quality of life of patients treated with existing drugs. Studies carried out in our laboratory demonstrated that administration of double the maximum tolerated dose of irinotecan (200 mg/kg/d x 3) in rats yielded 100% lethality within 7 days of treatment with irinotecan. In contrast, when the same dose of irinotecan was combined with celecoxib, a cyclooxygenase (COX-2) inhibitor (30 mg/kg), 100% survived with no significant **diarrhea.** Furthermore, in rats bearing advanced ward colorectal tumor (3 gm), irinotecan yielded no significant tumor responses, while the combination with celecoxib yielded an overall response rate of 75% (50% PR and 25% CR). Studies are continuing to

confirm the generalizability of this finding with other drugs and in other rodents bearing transplantable human tumors and to delineate the underlying mechanisms. These data preclinically provide a clear demonstration of improved therapeutic index of irinotecan by celecoxib and provide the basis for the design of the proposed phase I clinical trial with parallel laboratory investigations. The underlying hypotheses: 1) celecoxib protects selectively normal tissues; 2) down regulation of COX-2 by celecoxib in normal tissues results in selective restoration of the proliferation and amelioration of irinotecan toxicity; and 3) celecoxib protects against irinotecan-induced toxicity without altering the active irinotecan metabolite SN-38 to the inactive SN-38 glucuronide ratio. The specific aims are: 1) determine the maximum tolerated dose of irinotecan combined with celecoxib 400 mg PO BID. 2) assess the incidence of irinotecan-induced **diarrhea** in patients receiving weekly irinotecan in combination with celecoxib at 400 mg PO BID 3) Obtain pre-treatment and post-treatment evaluation of the following biological correlates in patients receiving irinotecan single agent or a combination of irinotecan and celecoxib: a) COX-2 expression; b) histopathologic evaluation with focus on mucosal damage and inflammation; and c) intestinal mucosal apoptosis; and 4) Evaluate the effect of celecoxib on the pharmacokinetic parameters of irinotecan and its metabolites. A collaborative team of scientists, medical oncologists, and pathologists is in place to assure that the proposed studies will be carried out efficiently. If we are successful in fulfilling the objectives of the proposed plan, the generalization of this approach can be tested with other drugs and other malignancies where impact on therapeutic outcome can be evaluated in phase II clinical trials.

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- **Project Title: KALLIKREIN KININ SYSTEM IN INFLAMMATORY BOWEL DISEASE**

  Principal Investigator & Institution: Colman, Robert W.; Director; Thrombosis Research Center; Temple University 406 Usb, 083-45 Philadelphia, Pa 19122

  Timing: Fiscal Year 2001; Project Start 30-SEP-1992; Project End 31-MAR-2003

  Summary: We have shown that bacterial products (proteoglycan-polysaccharide, PG-APS) found in the lower bowel produce chronic granulomatous inflammation similar to Crohn's disease (regional ileitis) in genetically susceptible rats as well as associated systemic inflammation. Activation of the contact system (CS) in plasma produces plasma kallikrein which activates neutrophils, cleaves high molecular weight kininogen (HK) and releases bradykinin which induces pain, swelling, **diarrhea,** and muscle contraction, all of which are characteristic symptoms of intestinal inflammation. We have shown that the CS activates mediates acute and chronic phases of intestinal inflammation in susceptible Lewis rats and is selective activated in these rats, but not in the resistant Buffalo rats. A specific kallikrein inhibitor decreases CS activation, acute inflammatory changes (edema, neutrophil infiltration), chronic intestinal inflammation and the systemic complications (arthritis, splenomegaly, hepatomegaly, leukocytosis, and the acute phase reaction. We have recently shown that there is a molecular difference between the plasma kininogen from Lewis rats which results in more rapid cleavage to yield bradykinin than in Buffalo rats. This proposal will test two hypotheses: (1) genetic differences between kininogen in susceptible and resistant rats result in selective activation of the Plasma Cs mediating certain of the pathological changes; (2) locally, intestinal tissue kallikrein is released and contributes to inflammatory changes. We will define the relationship of the single amino acid change to the functional consequences. In the view of the efficacy of plasma kallikrein inhibitors in blocking enterocolitis, we will use recombinant HK derivatives and peptides derived from HK

which can distinguish in vitro whether plasma kallikrein stimulation of neutrophils or bradykinin actions are responsible. In vivo, we will use kinin receptor blockers to define the mechanisms responsible for the enterocolitis. If bradykinin (BK) is responsible, then BK receptor blockers already used in clinical trials may merit evaluation in the therapy of chronic granulomatous enterocolitis. If plasma kallikrein is responsible, the development of plasma kallikrein inhibitors should be pursued. We will study the effect of total kininogen deficiency on the development of acute and chronic enterocolitis and systemic inflammation. Our recent studies show that tissue kallikrein (TK) is localized in macrophages of chronic granulomas and that TK may be secreted from inflamed intestinal cells. We will assay low molecular weight kininogen, the substrate of Tk using a newly designed assay as well as the natural protease inhibitor of TK. We will study the behavior of the TK system in intestinal cell lines and macrophages stimulated with PG-APS or inflammatory cytokines. In vivo, we will use a new specific TK inhibitor to attempt to modulate intestinal and systemic inflammation. These studies should demonstrate important mechanisms in the pathogenesis of inflammatory bowel disease. Assays of the CS and/or TK systems could distinguish active form inactive disease. In addition, the inhibitors used alone or in combination could serve in the future as potential therapeutic agents of human disease.

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- **Project Title: LONG-TERM IMPACT AND INTERVENTION FOR DIARRHEA IN BRAZIL**

  Principal Investigator & Institution: Guerrant, Richard L.; Professor; Internal Medicine; University of Virginia Charlottesville Box 400195 Charlottesville, Va 22904

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

  Summary: Having defined the magnitude, major new etiologies, key novel mechanisms and short-term impact of persistent diarrheal illnesses and even certain "asymptomatic" enteric infections in a model collaboration and cohort of children born into active prospective surveillance in an urban shantytown in Northeast Brazil, we are now have a unique opportunity to define for the first time the long-term DALY (disability adjusted life years) impact of early childhood enteric infections on nutritional status defined by anthropometry, physical activity and fitness, and cognitive function over extended periods (even years later). We postulate, based on our short-term impact data, that the greatest long-term impact will occur in children with persistent diarrheal illnesses and in those with low height-for-age Z (HAZ) scores. Having also shown the potential short-term benefits of a new glutamine-based oral rehydration and nutrition therapy (ORNT) and of vitamin A (with studies of zinc pending) on speeding the repair of damaged intestinal barrier function, we can now determine the potential long-term benefits of glutamine-based ORNT, with vitamin A and zinc therapy (targeting children with persistent **diarrhea** or reduced HAZ, as noted above). We shall also examine the intermediate (ie 1- 6 months) and long-term (greater than 6 months) effects of specific emerging enteric infections we have found to be important, enteroaggregative E. coli, and Cryptosporidium parvum. Coupled with our new developments of stable glutamine derivatives, the above data on full long-term DALY impact of persistent **diarrhea,** enteric infections and malnutrition, and the data on benefits of glutamine-based ORNT with vitamin A and zinc will ultimately allow us to calculate a much more meaningful cost-effectiveness (in "dollars per DALY averted) of selected treatment of high risk children (ie any with a persistent diarrheal illness that extends greater than 14 days, or a height for age Z score of less than 0.5). This model, longstanding collaboration and prospective field cohort surveillance will also enable the use of molecular tools

currently being developed to define the epidemiology and microbiology of such newly recognized major agents as enteroaggregative E. coli as well as opening new opportunities to train both US and international scientists in highly relevant bench and field investigation. This pioneering work builds on our unique opportunity to define for the first time the potentially huge (developmental and economic) burden of early childhood enteric infections, as well as holding promise for demonstrating a key intervention targeted at the most vulnerable subset of the population in greatest need.

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

- **Project Title: MECHANISM AND THERAPIES FOR HAART INDUCED DIARRHEA**

  Principal Investigator & Institution: Sipos, Tibor; President; Digestive Care, Inc. Ben Franklin Technology Center Bethlehem, Nj 18015

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

  Summary: (provided by applicant): The overall objective of this project is to establish the scientific rationale for the exogenous administration of a bicarbonate-buffered and enteric-coated pancrelipase to human immunodeficiency virus (HIV) positive patients who experience **diarrhea** due to High Activity Antiretroviral Therapy (HAART). As a side effect of HAART, many HIV patients experience mild to severe **diarrhea** with greasy and oily stool that is similar to the one experienced by cystic fibrosis (CF) patients. Drug induced **diarrhea** causes maldigestion of food, malabsorption of fat-soluble vitamins and nutrients, reduces the absorption of exogenously administered drugs, and leads to reduced immunocompetence. The technical approach for establishing the scientific rationale for the use of a bicarbonate-buffered and enteric-coated pancrelipase for the treatment of **diarrhea** and steatorrhea in HIV positive patients is to demonstrate that the HAART drugs interfere with any one of the key digestive processes that are responsible for handling the breakdown of fats and lipids, i.e., lipase/colipase and enterokinase catalyzed activation of zymogens to active enzymes. To achieve this goal the inhibitory effect of HAART drugs on pancreatic lipase/colipase, proteases and activation of prolipase to active lipase will be determined by employing specific enzyme assays. The results of these inhibitory studies will help to elucidate how these antiretroviral drugs interfere with the digestive activity of pancreatic lipase/colipase and the zymogen activation cascade that leads to HAART induced **diarrhea** and steatorrhea. Furthermore, the information gained from these in vitro studies will establish the therapeutic rationale for initiating the Phase II clinical program. The objective of the Phase II program is to demonstrate the efficacy of the exogenously administered bicarbonate-buffered and enteric-coated pancrelipase to HIV positive patients for the treatment of **diarrhea** due to HAART. PROPOSED COMMERCIAL APPLICATION: NOT AVAILABLE

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

- **Project Title: MODULATION OF HOST SIGNALING FUNCTIONS BY YERSINIA YOPS**

  Principal Investigator & Institution: Bliska, James B.; Associate Professor; Molecular Genetics & Microbiol; State University New York Stony Brook Stony Brook, Ny 11794

  Timing: Fiscal Year 2001; Project Start 01-FEB-2000; Project End 31-JAN-2005

  Summary: (Adapted from the Applicant's Abstract): The human-pathogenic Yersinia spp. (Y. pestis, Y. enterocolitica, and Y. pseudotuberculosis) are responsible for a range of diseases including **diarrhea,** mesenteric lymphadenitis, and bubonic plague. These bacteria invade into and colonize the lymphatic organs of humans and a variety of

animal hosts. Colonization of a host by Yersinia requires the function of a plasmid-encoded contact-dependent type III secretion system. This type III system translocates a set of toxic proteins known as Yops into host cells. The Yops impair normal host cell signaling functions, resulting in inhibition of phagocytosis, suppression of cytokine synthesis, and induction of apoptosis. The long-term goal of this grant is to understand how Yops modulate host cell signaling functions. The investigators will focus their studies primarily on YopH, a protein tyrosine phosphatase that inhibits phagocytosis, and YopJ, a protein that prevents cytokine synthesis and induces apoptosis. The first specific aim is to carry out a structure/function analysis of an amino-terminal domain in YopH that mediates translocation and substrate recognition. A combination of biophysical and genetic approaches will be used to achieve this goal. The second specific aim is to examine the mechanism of substrate recognition by YopH inside host cells. Animal and cultured cell infection assays will be used to study the behavior of genetically-altered YopH proteins in vivo. The third specific aim is to analyze the interaction of YopJ with host target proteins and to elucidate its mechanism action. Mutant forms of YopJ unable to bind target proteins will be generated and analyzed for biological activity in animal and cultured cell infection assays. The possibility that other Yops modulate the activities of mitogen-activated protein kinases in host cells will also be explored. As type III secretion pathways are important virulence determinants in a large number of bacterial pathogens, and the Yops provide an extremely powerful system to study pathogen interference with host signaling functions, these studies will aid the development of new strategies to combat a variety infectious diseases.

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- **Project Title: MOLECULAR BASIS OF SECRETORY DIARRHEA**

  Principal Investigator & Institution: Cohn, Jonathan A.; Associate Professor; Medicine; Duke University Durham, Nc 27706

  Timing: Fiscal Year 2001; Project Start 01-AUG-1999; Project End 31-DEC-2003

  Summary: In secretory **diarrhea,** the protein mainly responsible for controlling electrolyte and water movement into the intestinal lumen is the cystic fibrosis transmembrane conductance regulator (CFTR). CFTR functions as a Cl- channel subject to regulation by protein kinase A (PKA) and protein kinase C (PKC). CFTR activation requires phosphorylation by PKA and ATP hydrolysis, events occurring in adjacent CFTR domains termed nucleotide binding domain 1 (nbd1) and the R domain. This project will use recombinant peptides to study how CFTR is regulated. Peptides containing CFTR(62O-830), termed RD's, will model the R domain, and peptides containing CFTR(417-830), termed NBD/RD's, will model the nbd1/R domain. Modified peptides will contain Ala or Asp substitutions at one or more Ser residues. The project has three aims: AIM #1 will use RD's to study how protein kinases act on the R domain. Phosphorylated RD's will be analyzed by tryptic mapping and HPLC/mass spectrometry to identify phosphorylation events accompanying maximal vs. partial stimulation of CFTR. Additional studies will examine the mechanism by which protein kinases act on RD's and will determine how synergism between protein kinases orchestrates the orderly phosphorylation of CFTR. AIM #2 will study how PKA controls the intrinsic function of the nbd1/R domain. Pilot studies indicate that NBD/RD's exhibit PKA-regulated ATPase activity. These peptides will be used to determine which RD phosphorylation events activate vs. inhibit the nbd1 ATPase, to test whether the regulation of nbd1 by PKA is affected either by PKC or by nbd2, and to test whether the nbd1 ATPase is affected by the deltaF5O8 mutation, the most common cause of cystic fibrosis (CF). Aim #3 will study how protein kinases control the ability of the R domain

to activate the Cl- channel function of CFTR. RD's will be added to membrane patches containing a truncated CFTR lacking most of the R domain (deltaR/S66OA CFTR) to compare the ability of different modified RD's to regulate CF transport by CFTR. This project's long-term goal is to clarify how protein kinases act on the nbd1/R domain to regulate CFTR function. Detailed knowledge of CFTR regulation will be fundamental to developing pharmacological strategies to selectively augment or diminish CFTR function. Given the pivotal role of CFTR in the pathogenesis of **diarrhea** and CF this project has excellent prospects of leading to information of practical benefit in the treatment of these conditions.

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- **Project Title: MOLECULAR BIOLOGY OF THE ROTAVIRUSES**

  Principal Investigator & Institution: Estes, Mary; Professor; Molecular Virology & Microbiol; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2001; Project Start 01-AUG-1981; Project End 31-JAN-2006

  Summary: Rotaviruses are the major cause of life-threatening diarrheal disease in infants and animals worldwide. The long-term research objective of this laboratory is to understand the molecular biology of rotavirus protein function as it relates to mechanisms of pathogenesis and virus assembly. These complex viruses, which lack an envelope, have a unique morphogenetic pathway involving immature particle budding through membranes of the endoplasmic reticulum (ER). Recent studies of the role of nonstructural protein NSP4 in viral morphogenesis led to the discovery that this protein affects calcium homeostasis and functions as an enterotoxin. These studies suggest that NSP4 plays a key role in rotavirus pathogenesis by triggering a cell-signaling pathway that results in **diarrhea.** A cleavage product of NSP4 that is secreted into the medium of virus-infected cells retains enterotoxin activity. Intracellular NSP4 triggers a distinct signaling pathway that remains to be characterized. Antibody to NSP4 induces broadly cross-protective immunity against rotavirus-induced **diarrhea** in mice. Thus, NSP4 is clearly an important virulence factor, and virus-induced signaling plays a previously unrecognized role in rotavirus pathogenesis. This grant application proposes studies to understand the molecular details of viral and cellular functions critical for rotavirus pathogenesis. The specific aims of the proposed work are: (1) to dissect the pleiotropic properties of NSP4 by examining the effect of extracellular NSP4 on uninfected epithelial cells; (2) to examine the effects of intracellular NSP4 expression on epithelial cell function; and (3) to understand the role of NSP4 in the morphogenetic process in which virus particles bud through the ER membrane and acquire outer-capsid proteins VP4 and VP7. These studies will provide a molecular foundation to understand rotavirus pathogenesis and viral budding through ER membranes. Understanding these unique aspects of rotavirus pathogenesis offers opportunities to develop new strategies to prevent and control rotavirus disease in children and animals and understand fundamental exocytic processes of eukaryotic cells.

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- **Project Title: MOLECULAR EPIDEMIOLOGY AND IMPACT OF HUMAN ASTROVIRUSES**

  Principal Investigator & Institution: Mitchell, Douglas K.; Pediatrics; Eastern Virginia Medical School Norfolk, Va 23507

  Timing: Fiscal Year 2001; Project Start 01-SEP-2000; Project End 31-AUG-2005

Summary: Astroviruses cause 2-17 percent of the **diarrhea** episodes that require medical care in children. Our current understanding of the molecular epidemiology, seroprevalence, and immune response to astrovirus has been derived from limited studies from a variety of locations. Additional data are needed to determine if the prevention strategy of vaccine development is warranted. This study will describe attributes of human astroviruses (HAstVs) in two well-defined surveillance studies. The hypotheses of this study are that multiple HAstV antigenic types and strains are present simultaneously in a community, that type-specific immunity provides protection from symptomatic infection, and that HAstV illness results in an economic burden sufficient to warrant development and implementation of protective strategies. The specific aims of this study are: 1) To characterize the antigenic and genetic diversity of HAstVs among children in two prospective surveillance studies including hospitalized children in three locations of the U.S. and children in Mexico City under a community-based surveillance. 2) To characterize the immune response to HAstV among naturally infected children from these populations by measuring type- specific anti-HAstV antibody. 3) To determine the role of serum antibody in protection of children from symptomatic infection, and to determine whether the protection is type-specific or group-specific. 4) To determine if the burden of disease is sufficient to develop a vaccine by evaluating the economic impact of severe HAstV **diarrhea** among children in three U.S. cities over two years of surveillance. Information regarding type variability, genomic variability, molecular epidemiology, and type-specific immune response to astrovirus are necessary to develop preventive measures including immunization strategies.

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- **Project Title: MOLECULAR GENETICS OF ENTEROPATHOGENIC E COLI ADHESION**

  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-JUL-1986; Project End 31-MAR-2004

  Summary: (Adapted from the Applicant's Abstract): Enteropathogenic Escherichia coli (EPEC) are an important cause of **diarrhea** in infants. The long-term objectives of this project are to understand the pathogenesis of disease due to this organism and to develop diagnostic reagents and vaccine candidates for prevention of disease due to this pathogen. There are also many similarities between the pathogenesis of EPEC and the intestinal pathogenesis of enterohemorrhagic (Shiga toxin- producing) E. coli O157:H7 (EHEC) which have been responsible for many large outbreaks of bloody **diarrhea** and hemolytic uremic syndrome (HUS) in the U.S. and elsewhere due to the ingestion of contaminated beef, water, apple cider, and other vehicles. Dr. Kaper has shown that there is genetic similarity between some intestinal virulence factors of EPEC and EHEC and information resulting from the proposed studies will also yield insights into the pathogenesis of EHEC. The pathognomonic intestinal histopathology associated with EPEC infection is the attaching and effacing (A/E) lesion where brush border microvilli are effaced, the bacteria are intimately attached to the epithelial cell membrane, and high concentrations of polymerized actin accumulate beneath the adherent bacteria. Previous work supported by this project has revealed that the A/E histopathology is encoded on a 35 kb pathogenicity island called LEE for Locus of Enterocyte Effacement. This pathogenicity island encodes a type III protein secretion system, and transfer of the LEE into E. coli K-12 confers the A/E phenotype upon this avirulent host strain. In the next period of support, Dr. Kaper proposes to further characterize the functions of genes contained within the LEE. There are four specific aims for the proposed studies: 1)

Characterize heretofore cryptic genes of the LEE, particularly those genes potentially encoding secreted proteins; 2) Further characterize the type III secretion system encoded on the LEE; 3) Study the regulation of the LEE-encoded genes and the effect of the Per transcriptional activator; 4) Clone and characterize the gene(s) encoding the initial EPEC adhesin that is responsible for initial binding to human intestinal tissue cultured in vitro. The proposed experimental approach will use a combination of molecular genetics, cell biology, and animal studies to achieve a better understanding of how EPEC infects intestinal epithelial cells and causes disease.

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- **Project Title: MOLECULAR MECHANISMS OF CFTR REGULATION**

  Principal Investigator & Institution: Ladias, John A.; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

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

  Summary: (provided by applicant): The cystic fibrosis transmembrane conductance regulator (CFTR) is an ATP-regulated chloride channel that determines the rate of electrolyte and fluid transport in the apical membrane of epithelial cells. Abnormal CFTR function is associated with the pathogenesis of cystic fibrosis and secretory **diarrhea.** Our long-term objective is to understand the molecular mechanisms underlying the regulation of CFTR at the atomic level and develop novel strategies for modulating the activity of this channel and treating the CFTR-associated diseases. The CFTR topology consists of two membrane-spanning domains and five cytoplasmic domains: an N-terminal domain (NTD), two nucleotide-binding domains, a regulatory domain (R) and a C-terminal domain (CTD). The CFTR activity is modulated through phosphorylation of the R domain, ATP hydrolysis by the NBDs, and interactions of its NTD and CTD domains with syntaxin 1A and NHERF proteins, respectively. However the regulatory mechanisms remain unknown primarily because the three-dimensional structure of the CFTR domains and the structural basis of their interaction with intracellular regulatory proteins remain elusive. This proposal addresses these questions and focuses on the structural analysis of cytoplasmic CFTR domains and their complexes with regulatory proteins, using molecular biology techniques and X-ray crystallography. The specific aims are: 1. To dissect the structural basis of CFTR channel gating mediated through the interaction of the CFTR CTD with the NHERF PDZ1 and PDZ2 domains. 2. To elucidate the molecular mechanisms underlying the regulation of CFTR channel activity through the interaction of the CFTR NTD with syntaxin 1A. 3. To determine the three-dimensional atomic structures of the CFTR NBD1 and NBD2 domains. These studies will provide the first high-resolution three-dimensional structures of four cytoplasmic CFTR domains and the structural basis of CFTR regulation by proteins syntaxin 1A and NHERF. This information is an essential step towards elucidating the basic molecular mechanisms that control the CFTR channel gating. Importantly, the atomic coordinates of these complexes could be used for structure-based rational design of drugs that would modify selectively the CFTR activity with clinical applications in the treatment of cystic fibrosis and secretory **diarrhea.**

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- **Project Title: MOLECULAR PHYSIOLOGY OF BAND 3 LIKE PROTEINS OF KIDNEY**

  Principal Investigator & Institution: Alper, Seth L.; Professor; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

Timing: Fiscal Year 2001; Project Start 15-JAN-1991; Project End 31-MAR-2003

Summary: (Adapted from the Applicant's Abstract): The AE anion exchanger gene family encodes complex polytopic transmembrane polypeptides that contribute to regulation of intracellular pH (pHi), cell [Cl-], and cell volume through their mediation of electroneutral Cl-/HCO3- exchange. AE-mediated Cl-/HCO3- exchange in polarized epithelia also regulates secretion and reabsorption of proton equivalents and of Cl-. AE-mediated Cl-/HCO3-exchange is thought to be of widespread physiological importance in many cell types. AE1 deficiencies have been particularly associated with hereditary syndromes of spherocytic anemia and of distal renal tubular acidosis. Deficiencies of AE2 or AE3 activity have yet to be defined. Deficiency of a different Cl-/HCO3-exchange activity leads to congenital chloride **diarrhea.** This competitive continuation grant application proposes to extend past and current experiments by pursuit of the following Specific Aims: 1. Further define structural loci of the regulatory differences among AE isoforms, especially AE1 and AE2. 2. Study natural variants of the AE genes and a different class of anion exchanger for clues about ion translocation pathways and mechanisms. These will include: a. AE1 mutations that cosegregate and likely contribute to heritable distal renal tubular acidosis b. AE polypeptides of genetically related fish that live in river or in soda lake environments c. a more distantly related member of the bicarbonate-transporter superfamily cloned from yeast d. the unrelated sulfate transporter DRA that when mutated results in congenital chloride **diarrhea.** 3. Further compare and define the mechanisms of electroneutral and electrogenic anion exchange mediated by AE1 E699Q and likely mediated by AE2 E1007Q. 4. Apply directed mutagenesis to define the residues of AE1 and AE2 that contribute to binding and transport of substrate anions and to deduce constraints on secondary and tertiary structure of AE polypeptides. 5. Define aspects of transcriptional and translational regulation of AE gene products in kidney of mutant and parental mouse strains and in cultured kidney cells.

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- **Project Title: NEW PARADIGMS OF CFTR REGULATION**

  Principal Investigator & Institution: Kirk, Kevin L.; Professor; Physiology and Biophysics; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2001; Project Start 01-SEP-2000; Project End 31-AUG-2005

  Summary: (Adapted from the Applicant's Abstract): The CFTR chloride channel is implicated in two major human diseases: cystic fibrosis (low CFTR activity) and secretory **diarrhea** (excessive CFTR activity). The development of rational treatment strategies for either disease requires a better understanding of what activates or inactivates the CFTR channel. Although it is clear that CFTR is stimulated by PKA-mediate phosphorylation of the large regulatory domain (R domain) within this channel, the mechanisms that control CFTR gating are still obscure. Two new paradigms of CFTR regulation will be explored: 1) the stabilization of CFTR channel activity by an intramolecular interaction between the amino-terminal tail (N-tail) and the R domain and 2) the coupling of CFTR gating to the membrane traffic machinery by an intermolecular interaction between the CFTR N-tail and syntaxin 1A. These paradigms will be explored by pursuing three Specific Aims. First, the mechanism by which the N-tail stabilizes CFTR channel activity will be defined. Subaims include testing the hypothesis that the N-tail controls channel gating by modulating the phosphorylation of key residues within the R domain. Second, the structural basis of the interaction between the N-tail and R domain will be defined. The nature of the physical interaction between these domains will be characterized and the hypothesis that CFTR channel

gating can be disrupted by peptides that block this interdomain interaction will be tested. Third, the hypothesis that CFTR channel gating is regulated by interactions between this ion channel will be tested and that components of the membrane traffic machinery coordinate the regulation of ion transport and protein traffic in epithelial cells. The results of the proposed study should provide new information regarding the mechanisms that control the activity of the CFTR chloride channel; information that may lead to more effective strategies for manipulating CFTR function in diseases that involve this ion channel.

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- **Project Title: NO& EPITHELIAL REPAIR IN CRYPTOSPORIDIOSIS**

  Principal Investigator & Institution: Gookin, Jody L.; Anatomy/Physiological Scis Rad; North Carolina State University Raleigh 2230 Stinson Drive Raleigh, Nc 27695

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

  Summary: The Research Proposal: The long-term goal of these laboratories are to better understand the cellular mechanisms of **diarrhea** and tissue injury, define the integrated mechanisms of mucosal defense and repair in infectious enteritis, and identify rational approaches to nutritional and pharmacologic enhancement of epithelial repair. Our preliminary studies showed that inducible nitric oxide synthase is expressed intensely by damaged enterocytes after acute mucosal bile salt injury. Exogenous L-arginine promotes epithelial repair after the injury; an effect that depends upon NO synthesis. The present studies hypothesize that iNOS is a key mediator of epithelial defense and repair in Cryptosporidium infection by hastening elimination of infected enterocytes and restitution. We will use a well-characterized experimental model of neonatal porcine cryptosporidiosis and migration studies of porcine jejunal enterocytes to examine the role of NOS in epithelial injury and restitution at both the cellular and whole tissue level and in the presence and absence of inflammatory mediators. The Candidate is a veterinarian who has completed a residency in Internal Medicine and is a board certified Diplomate of the American College of Veterinary Internal Medicine. The candidate has also completed a Ph.D. in Physiology with a minor in Biotechnology. The dissertation examined the role of L-arginine and prostaglandins in restoration of mucosal barrier function after acute mucosal bile salt injury. As a veterinary internist and gastrointestinal physiologist, the candidate is committed to a career in academia pursuing basic research, with a lesser commitment to clinical service and teaching. The Environment: The sponsor and co-sponsors of this proposal each can provide unique contributions to the proposed research and professional development of the candidate. The laboratories in which the candidate is engaged are capable of providing the room, equipment, animal handling facilities, and support staff necessary for completion of this proposal. The laboratories are contained within the College of Veterinary Medicine (NCSU) and School of Medicine (UNC) which provides intensive interdisciplinary training and support through the Core Center for Gastrointestinal Biology and Disease, Biotechnology Program, seminars, and journal clubs.

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

- **Project Title: NSP4 STIMULATED ION CHANNELS AND AGE-DEPENDENT DIARRHEA**

  Principal Investigator & Institution: Morris, Andrew P.; Integr Biol/Pharm/Physiology; University of Texas Hlth Sci Ctr Houston Box 20036 Houston, Tx 77225

  Timing: Fiscal Year 2002; Project Start 15-FEB-2002; Project End 31-JAN-2007

Summary: (provided by applicant): Rotaviruses are a major cause of life-threatening **diarrhea** in infants and children worldwide. Following viral infection, **diarrhea** is seen associated with pathophysiological changes in mucosal fluid and electrolyte balance. My group has focused on defining a new pathophysiological component to **diarrhea.** We have shown that a rotaviral non-structural protein called NSP4 induces **diarrhea** in both normal and cystic fibrosis mouse pups accompanied by calcium-sensitive chloride secretory current generation by gastrointestinal mucosa. Neither **diarrhea** nor anion secretion occur in adult mice. At the sub-cellular level, NSP4 causes phospholipase C sensitive intracellular calcium (Ca2+)i mobilization and calcium-sensitive halide influx into mucosal crypts. NSP4-induced (Ca2+)i mobilization (our assay for receptor occupancy) is not age-dependent. Thus, we hypothesize that NSP4 activates and age-dependent calcium-sensitive chloride channel in pup mucosa causing chloride secretion, and secretory **diarrhea.** We propose studies in native cells to identify and characterize the electrophysiological and pharmacological properties of the chloride channel, and thus unequivocally demonstrate a role for this conductance in NSP4 mediated age-dependent cellular halide influx. We intend to identify the cellular signaling mechanisms coupling NSP4 mediated changes in (Ca2+)i to this conductance. These mechanistic studies may identify novel targets for pharmacological intervention with clear clinical relevance. These goals will provide the cellular basis for the age-dependent secretory **diarrhea** and may identify a molecular target for rotaviral-induced transepithelial anion secretion. They will also translate facts established for the biophysics of calcium-activated chloride channel expression in cultured epithelial cell-lines into the fields of clinical medicine and disease. In doing so, our results will provide an excellent possibility for development of new therapies for rotaviral gastroenteritis, and for other infectious diseases in children where altered mucosal (Ca2+)i homeostasis occurs.

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- **Project Title: NURSING MANAGEMENT OF IBS: IMPROVING OUTCOMES**

  Principal Investigator & Institution: Heitkemper, Margaret M.; Professor & Director; Biobehavioral Nursing and Health Systems; University of Washington Seattle, Wa 98195

  Timing: Fiscal Year 2003; Project Start 01-AUG-1996; Project End 31-JAN-2007

  Summary: (provided by applicant): The proposed application is a competitive supplement to the NINR funded project titled "Nursing Management of IBS: Improving Outcomes". In the United States, it is estimated that 10-20% of the population experience symptoms compatible with a diagnosis of irritable bowel syndrome (IBS). IBS is a functional condition characterized by change in bowel patterns, (e.g., constipation, diarrhea), interfering with functional activities and increasing health care utilization. Current recommended therapies include diet manipulation, self-management, psychotherapy, and motility and pain modulation via pharmacological therapy. The purpose of the parent project funded in 2002 is 1) to determine whether the CSM intervention is equally effective in men and peri- and postmenopausal women and 2) to determine whether the CSM intervention is as effective when delivered over the telephone as compared to a face-to-face approach. A three-group randomized clinical trial with longitudinal follow-up will be used to test the effectiveness of a face-to-face versus telephone comprehensive self-management (CSM) program relative to a usual care control group. Outcome variables will be measured during the assessment phase (T1) then 6 months (T2) and 12 months (T3) after the randomization phase. The primary aim of this supplement is to compare the distribution of SET polymorphisms across predominate bowel pattern subgroups and gender in people with IBS. We hypothesize

that the distribution of SERT polymorphisms (5'-flanking promoter region [5-HTTLPR] and in exon 2 [VNTR]) will differ across predominate bowel pattern subgroups and the distribution of SERT polymorphisms will differ by gender. Exploratory aims of this study include: 1) Evaluate the relationship of SERT polymorphisms to symptom experiences and psychological profile; 2) Test whether the degree of improvement in response to the CSM therapy differs by SERT polymorphism; and 3) Evaluate the relationship of platelet rich plasma 5-HT levels to SERT polymorphisms, predominate bowel pattern. This study will provide information on the potential role of serotonin processing in IBS as well as potential gender and bowel symptom predominance. Such results may ultimately be used to tailor therapies for this common health problem.

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- **Project Title: PATHOGENESIS OF CAMPYLOBACTER ENTERITIS:**

  Principal Investigator & Institution: Konkel, Michael E.; Microbiology; Washington State University 423 Neill Hall Pullman, Wa 99164

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

  Summary: (provided by the applicant): The ultimate goal of this research is to use the knowledge gained from the identification and characterization of Campylobacter jejuni virulence determinants to reduce morbidity and mortality resulting from C. jejuni infections. C. jejuni is a leading cause of human gastrointestinal disease worldwide, causing approximately 3.5 million cases of diarrheal illness per year in the United States. Infection with C. jejuni is characterized by fever, severe abdominal cramps, and **diarrhea** containing blood and leukocytes. The dysenteric nature of Campylobacter infection, coupled with experimental evidence, supports the notion that C. jejuni must invade the cells lining the gastrointestinal tract for the development of C. jejuni-mediated enteritis. The focus of this proposal is to identify and functionally characterize the bacterial proteins necessary for C. jejuni internalization. Previous work in my laboratory has revealed that C. jejuni synthesize and secrete proteins upon co-cultivation with mammalian cells. These secreted bacterial proteins have been collectively called Campylobacter invasion antigens (Cia). A mutation in a gene encoding the 73 kDa CiaB secreted protein results in a non-invasive phenotype. I hypothesize that Cia proteins are secreted via a Type III export pathway from C. jejuni. The results of this research will better define the pathogenic mechanisms and virulence determinants of one enteric pathogen, C. jejuni, and will be useful in the development of intervention and control methods to reduce the number of cases of human campylobacteriosis.

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

- **Project Title: PATHOGENESIS OF ETEC INFECTIONS**

  Principal Investigator & Institution: Fleckenstein, James Michael.; Medicine; University of Tennessee Health Sci Ctr Health Science Center Memphis, Tn 38163

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

  Summary: PROPOSAL (Adapted from the applicant's abstract): Enterotoxigenic Escherichia coli (ETEC) are a leading cause of infectious **diarrhea** worldwide, causing hundreds of thousands of deaths each year. There is presently no licensed vaccine to prevent infections caused by these organisms. Furthermore, many avenues of basic clinical investigation remain unexplored. The long-term objective of these studies is to discover viable candidates for ETEC vaccine development employing molecular pathogenesis studies to more fully understand the essential determinants of virulence.

All prior vaccine and pathogenesis studies to date have focused on extrachromosomal (plasmid)-encoded virulence factors. The studies proposed here attempt to capitalize on the recent discovery of a pathogenicity island (PAI) in the chromosome of the prototypical ETEC strain H10407, located in the selC gene, the site of two previously described PAIs in other pathogenic E. coli. At least two genes encoded on the island, tia and DleoA, affect virulence in an animal model of infection and modulate the release of a known critical virulence factor, the heat-labile toxin (LT). Understanding the events which facilitate the export and delivery of this toxin to its target receptors on eukaryotic cells could prove valuable in the ultimate development of an effective vaccine. The studies proposed herein focus primarily on the role of the PAI in modulating the release of LT. The outlined experiments concentrate on a specific locus within the PAI that contains open reading frames (ORFs) encoding putative proteins with motifs common to bacterial secretion systems. These studies are directed at ascertaining the role of these genes in modulating the synthesis and export of LT. Finally, experimental challenge studies will examine the contribution of the PAI to virulence of ETEC in human infection. Specific Aims: 1. Construction of in-frame deletions in selected genes located on the PAI. In this aim, the focus will be on ORFs within a putative secretion element of the PAI. The resulting collection of isogeneic deletion mutants will then be used in subsequent experiments directed at their phenotypic characterization. 2. Phenotypic characterization of isogeneic deletion mutants. Each mutant will be examined in a number of assays to investigate the effects of the deletion on toxin synthesis, export, and delivery to eukaryotic target molecules. These experiments will be used to confirm the investigator's hypothesis that additional genes of the PAI, which together encode a multicomponent membrane transporter, are required to modulate LT release. 3. Subcellular localization and characterization of proteins encoded by virulence genes on the PAI. While assessing the impact of each mutation on virulence and toxin release, the individual proteins will be characterized on a molecular level with experiments to define their subcellular location. These studies will be needed to validate the present hypothetical model of the role played by these proteins as LT is released from the periplasmic space of ETEC. 4. Testing of an in-frame deletion mutant in a human experimental challenge model of ETEC infection. To examine the contribution of the PAI to virulence of ETEC H10407, the DleoA in-frame deletion mutant will be tested in humans.

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- **Project Title: PHENOTYPE OF B CELLS INDUCED BY ROTAVIRUS INFECTION**

  Principal Investigator & Institution: Arvin, Ann M.; Professor of Microbiology and Immunology; Pediatrics; Stanford University Stanford, Ca 94305

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

  Summary: (provided by applicant) Rotaviruses (RVs) are the most important cause of severe dehydrating **diarrhea** in children in both developed and less developed countries. It is estimated that RV are responsible for the death of approximately 2000 children daily worldwide principally in developing countries. Studies in animals and in humans indicate that humoral immune mechanisms appear to be the primary determinants of protection from reinfection following wild-type disease or vaccination. Better methods are needed to characterize the qualitative and quantitative nature of the humoral immune response in children from developed and less developed countries. The proposed studies will be done primarily in Colombia- South America as an extension of NIH Grant: (R37 AI21362). Using B cell ELISPOTS and a novel flow cytometry assay we plan to quantify and study the phenotype of rotavirus specific B

cells induced after natural rotavirus infection in children and adults in Colombia, and in children after natural rotavirus infection and after administration of a rotavirus vaccine. We will study these lymphocytes for the presence of molecules implicated in lymphocyte homing to the intestinal mucosa and B cell maturation markers that will aide in differentiating effector vs. memory B cells. A practical long-term goal of this project is to find parameters that correlate with protection induced by rotavirus vaccines. Since rotaviruses replicate almost exclusively in the intestinal mucosa, another long-term goal of this project is to gain a better understanding of the molecular determinants of the immune response to rotavirus in particular, as well as a deeper understanding of the humoral mucosal immune response in general with specific emphasis on B cell memory and homing.

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

- **Project Title: REGULATION OF CALCIUM RELEASE IN INTESTINAL MYOCYTES**

  Principal Investigator & Institution: Bielefeldt, Klaus; Associate Professor; Internal Medicine; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2001; Project Start 24-AUG-1998; Project End 31-MAY-2003

  Summary: The normal gastrointestinal motility depends on a cascade of intracellular signals that translate a signal at the cell membrane into muscle contraction. The calcium ion plays a central role in this process of excitation-contraction coupling. Changes in the calcium homeostasis of smooth muscle cells may thus contribute to common gastrointestinal diseases, such as constipation, **diarrhea,** or gastroesophageal reflux disease. Increases in the cytosolic calcium level can be due to calcium influx through ion channels in the cell membrane or calcium release from intracellular stores. Two intracellular calcium release channels have been identified in intestinal smooth muscle cells: the inositol 1,4,5-trisphosphate receptor channel and the ryanodine receptor channel. Little is known about the mechanisms that modulate the activity of these intracellular calcium release channels. We hypothesize that ryanodine receptor channel isoforms are differentially expressed in gastro-intestinal smooth muscle from anatomically and functionally distinct areas; associated modulatory proteins further increase this heterogeneity, thereby affecting intestinal motor function. The proposed experiments will investigate the regulation of calcium release from intracellular stores. The following specific goals will be addressed: (1) Biochemical and functional characterization of calcium release channels expressed in intestinal smooth muscle cells. (2) Identification of proteins associated with ryanodine receptor channels in intestinal smooth muscle cells. (3) Characterization of the functional role of proteins associated with the ryanodine receptor channel. A better understanding of mechanisms that control the calcium homeostasis may provide important insight into the etiology of diseases or lead to the development of novel treatment strategies for functional abnormalities.

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

- **Project Title: ROLE OF GALANIN IN INTESTINAL PATHOPHYSIOLOGY**

  Principal Investigator & Institution: Benya, Richard V.; Medicine; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2001; Project Start 15-JUN-2000; Project End 31-DEC-2001

  Summary: This abstract is not available.

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

- **Project Title: S. TYPHIMIURIUM VACCINE AGAINST BACTERIAL ENTEROPATHOGENS**

  Principal Investigator & Institution: Curtiss, Roy Iii.; Professor; Biology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

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

  Summary: Of the 18.9 million annual deaths (1997) due to infectious diseases, about 2 million are the result of infections by Salmonella and other related bacterial enteropathogens including Escherichia coli and Shigella species, and less closely related enteropathogens such as Vibrio cholerae, Campylobacter jejuni and Listeria monocytogenes. In addition, these bacteria are responsible are responsible for significant morbidity causing diarrheal and systemic diseases that can be transmitted to humans by contamination of food products and/or the water supply and such contamination can be willful. In the belief that improving health, nutrition and economic well-being (the latter dependent on the first two) provide the best means to enhance the quality of life globally and thus reduce conditions that result in warlike and terrorist behavior, we propose a vaccine developmental program based on our recent technical developments in using non-recombinant and recombinant attenuated Salmonella veterinary vaccines to prevent-reduce diarrheal diseases caused by bacterial enteropathogens. Our objectives include: (i) to further genetically modify a strain of Salmonella typhimurium that has been designed to minimize induction of immune responses to serotype-specific antigens and to maximize induction of cross protective immunity to common related antigens of S. enterica strains of diverse serotype and then fully evaluate this modified strain as a vaccine to reduce diarrheal diseases in humans caused by S. enterica serotypes and possibly by other bacterial enteric pathogens, especially Escherichia coli of the EPEC, ETEC and EHEC types and Shigella; (ii) to design, construct and fully evaluate an attenuated derivative of S. paratyphi A, with similar genetic attributes as the S. typhimurium vaccine designed for the same purpose, to induce cross protective immunity in humans to prevent enteric fever and to significantly reduce diarrheal diseases due to infection by diverse S. enterica serotypes and possibly by other bacterial enteric pathogens, especially E. coli of the EPEC, ETEC and EHEC types and Shigella; (iii) to further genetically modify the S. typhimurium and S. paratyphi A vaccines designed to induce cross protective immunity to also display biological containment so that they are less able to survive in the intestinal tract or in nature and/or die by lysis after approximately ten cell divisions following delivery to the immunized individual; and (iv) to design, construct and evaluate recombinant attenuated Salmonella vaccines, using optimal attributes for immunogenicity, biological containment and antigen delivery, to express antigens to further enhance induction of cross protective immunity to Salmonella-related bacterial enteropathogens or to confer protective immunity to one of the less Salmonella-related enteropathogens. We will also collaboratively work to develop our Master File, prepare and fully characterize candidate vaccine Master Seeds for stability and safety, prepare and submit protocols for IRB approvals, submit information necessary to obtain INDs, and perform any other work needed to arrange that the best candidate vaccines by clinically evaluated in human volunteers.

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

- **Project Title: SHIGA TOXIN 1:UPTAKE MECHANISMS AND INTRACELLULAR ACTION**

  Principal Investigator & Institution: Kovbasnjuk, Olga N.; Medicine; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2003; Project Start 15-SEP-2003; Project End 31-AUG-2006

Summary: (provided by applicant): Foodborne diarrheal disease cause 76,000,000 cases each year in the United States. Intestinal pathology caused by Shiga toxin-producing Escherichia coli (EHEC), important food-borne pathogens, includes approximately 35% of all bloody **diarrhea** in the United States, an unknown % of watery **diarrhea,** and the life-threatening systemic manifestations (observed in up to 10% of cases) of infection, the hemolytic uremic syndrome (HUS) and encephalopathy. EHEC are the leading cause currently of acute and chronic renal failure in children in the USA. EHEC is a particularly worrisome foodborne pathogen, because the number of outbreaks caused by EHEC continue to significantly increase and there is no effective specific therapy for this illness which is lethal in up to 10% of children who develop HUS. Thus, there is a great need to better understand the pathogenesis of this infection to promote development of new therapeutic approaches to treat EHEC infection and its complications. Understanding the complex mechanism of Stx uptake and trafficking pathways into colonic epithelium may help to identify new drug targets and develop new strategies directed at preventing toxin action on human intestine. In this application we will study the mechanism of Stx1 and its B-subunit (Stx1B) uptake, trafficking and intracellular action using animal and human intestinal epithelial cell models. In Aim 1 we will study the role of lipid rafts (LR) in Stx1/Stx1B translocation across the apical cell surface. We propose to test the role of LR proteins, which are associated with toxin receptor in toxin translocation machinery. In Aim 2 we will study a newly recognized Stx1/Stx1B internalization pathway from plasma membrane into the nucleoli. In Aim 3 we will study the mechanisms of Stx1/Stx1B-induced apoptosis and its role in toxin-related intestinal inflammation. These proposed studies should provide new insight into the understanding of the molecular basis of Stx-mediated intestinal epithelial cell injury and facilitate the design of strategies to prevent Stx1 uptake and intracellular action, and thus serve to find new targets to interfere with EHEC-related gastrointestinal pathophysiology.

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

- **Project Title: SHIGA TOXIN MODE OF ACTION IN BACTERIAL DISEASE**

  Principal Investigator & Institution: Obrig, Tom G.; Research Professor; Internal Medicine; University of Virginia Charlottesville Box 400195 Charlottesville, Va 22904

  Timing: Fiscal Year 2003; Project Start 01-APR-1990; Project End 31-DEC-2007

  Summary: (provided by applicant): Shiga toxin-producing E. coil (STEC) is an emerging infectious pathogen that causes in excess of 30,000 cases of disease per year in the United States. STEC, including E. coil O157:H7, is also the leading cause of acute renal failure, hemolytic uremic syndrome (HUS), in young children. No effective preventive modality or therapeutic intervention is currently available for this disease. This project is designed to more fully describe a "window of opportunity" available for treatment and prevention of STEC-associated acute renal failure. In most cases, a three to nine day period of renal inflammation takes place between the appearance of bloody **diarrhea** and the onset of acute renal failure. It is believed that STEC virulence factors such as Shiga toxin (Stx2) and lipopolysaccharide (LPS) are the primary initiators of the renal disease. These factors elicit production of pro-inflammatory host cytokines and chemokines. This study utilizes a murine model to define the cytokines and chemokines involved and describe how these agents cause migration and accumulation of inflammatory cell types in the kidney. These cell types include neutrophils, monocytes/macrophages and platelets. Mice with mutated cytokine, chemokine, or adherence factor genes are to be employed to determine which of these factors are required in the disease process. In addition, adherence of these cell types to isolated

endothelial cells under flow conditions is included to define the inflammatory action of Stx2 and LPS. Studies are also included to show how host cytokines and chemokines further sensitize endothelial cells to Stx2 by activation of intracellular signal transduction pathways. The goal of these studies is to reveal the opportunities available for effective application of therapeutic agents in STEC-associated renal disease.

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

- **Project Title: SLOWING OF TRANSIT - THE THIRD ENTERIC FUNCTION OF 5-HT**

  Principal Investigator & Institution: Lin, Henry C.; Director Gastrointestinal Motility Progr; Cedars-Sinai Medical Center Box 48750, 8700 Beverly Blvd Los Angeles, Ca 90048

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

  Summary: (provided by applicant): In order to optimize nutrition, the movement of a meal through the small intestine must be precisely controlled to ensure that there is adequate time to complete the time-demanding steps of digestion and absorption. Abdominal pain, nausea, bloating, **diarrhea** and malnutrition are the consequences of impaired control of intestinal transit. After a fat-containing meal, inhibitory feedback mechanisms are activated by the proximal and distal small intestine as the jejunal and ileal brake, respectively. In contrast to this focus of the postprandial gut to slow transit, much of the research efforts over the past 100 years have been directed at the peristaltic reflex, which is responsible for the acceleration of intestinal transit and are known to be mediated by 5-HT. Currently, two roles of enteric 5-HT have been established: the triggering of the peristaltic and mucosal secretory reflexes via intrinsic primary afferent neurons and gut-to-CNS and gut-to-pancreas communications via extrinsic sensory nerves. We have recently found a third role of enteric 5-HT. Specifically, 5-HT is also involved in the slowing of transit by fat via a 5-HT3 pathway that is dependent on 5-HT transmission via myenteric neurons. In this proposal, we will test our overall hypothesis that slowing of intestinal transit by fat depends on primary afferent nerves, beta-adrenergic pathway and 5-HT transmission via myenteric neurons, which in turn activates opioid neurons, that slow transit. We will test the hypotheses using pharmacologic and physiologic approaches. The results of these studies will help us to refine our hypotheses so that we can test the neuroanatomic components of this pathway using immunohistochemistry. We have developed a collaboration with 2 leading neuroscientists who will provide this project with additional expertise in immunohistochemistry. In addition, to test the role of a novel beta-adrenergic system in the slowing of intestinal transit by fat, we have developed a multi-disciplinary team approach by including a cardiologist experienced in the 13- adrenergic system. The PI has a track record of success in bench-to-bedside translational research in the area of nutrient control of intestinal transit. His experience includes the discovery of a novel, nutrient-based strategy to slow intestinal transit. This application will bring this new treatment back to basic research so that we can understand the neural pathways that underpin the slowing response to fat. The hypotheses to be tested in this project will expand our understanding of a new role for enteric 5-HT which may explain conditions such as irritable bowel syndrome and provide better understanding of the effects of drugs that are directed at 5-HT pathways. In addition, by investigating the mediators of the control of intestinal transit, we will gain knowledge that can be used to control the movement of a meal through the small intestine and, in turn, reduce symptoms and improve nutrition.

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

- **Project Title: STCE, AN E.COLI O157:H7 PROTEASE SPECIFIC FOR C1-INH**

  Principal Investigator & Institution: Welch, Rodney A.; Professor & Chair; Medical Microbiol & Immunology; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2003; Project Start 16-JAN-2003; Project End 31-DEC-2007

  Summary: (Provided by applicant): Enterohemorrhagic Escherichia coli (EHEC), principally serotype O157:H7, cause an estimated 20,000 cases of diarrheal disease in the United States per year. 2-6 percent of the infected individuals, mostly young children progress to a severe renal disease, hemolytic uremic syndrome (HUS). The EHEC pathogenic factors that lead to bloody colitis and HUS are poorly understood, but knowledge of some mechanisms has recently emerged. Intimin-mediated adherence and type III effectors are encoded by a chromosomal locus termed LEE. The phage-encoded Shiga toxins (Stxs) are responsible for significant aspects of EHEC disease. EHEC strains commonly possess large plasmids, the prototype being pO157. We have identified a new pO157 gene, stcE, which encodes an extracellular zinc-metalloendoprotease (ZMP) that specifically cleaves the critical anti-inflammatory regulator C l-esterase inhibitor (C 1-Inh). C 1-Inh is a serine protease inhibitor (serpin) that provides the principal inhibition of the proteolytic cascades involved in classic and mannan-binding ligand complement activation, contact activation and intrinsic coagulation. C l-Inh inhibits diverse proteases: Clr and Cls, MASP-1, MASP-2, kallikrein, FXIIa, FXIa, and plasmin. Deficiencies in Cl-Inh cause profound clinical syndromes. The best known is hereditary angioedema (HAE), a genetic deficiency in Cl-Inh, which is characterized by transient, recurrent attacks of intestinal cramps, vomiting, **diarrhea** and life-threatening episodes of tracheal swelling. Fluorescenated StcE binds to cultured macrophages, B- and T-cells. Thus, StcE is an example of a growing class of ZMPs such as tetanus, botulinum and anthrax lethal factor toxins. These ZMPs, in contrast to the homologous Pseudomonas and Vibrio ZMPs, have specific, non-extracellular matrix protein targets. We will test the hypothesis that StcE degrades soluble or cell-associated Cl-Inh, and this results in poorly regulated serine protease cascades involving complement activation, contact activation and coagulation. This dysregulation would then contribute to local inflammation, tissue damage and edema. The elucidation of StcE structure and function(s) may result in new targets for chemotherapeutic or immune prevention or treatment of EHEC infections, which now are best managed only by supportive therapy.

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

- **Project Title: STRUCTURE-FUNCTION STUDIES OF FLAGELLAR ROTOR COMPONENTS**

  Principal Investigator & Institution: Blair, David F.; Associate Professor; Biology; University of Utah 200 S University St Salt Lake City, Ut 84112

  Timing: Fiscal Year 2001; Project Start 01-APR-2000; Project End 31-MAR-2004

  Summary: Many of bacteria swim by rotating helical filaments that act as propellers. This motility is a factor in the virulence of many bacterial pathogens, including those that cause ulcers, syphilis, burn wound infections, and some **diarrhea.** Each filament is driven by rotary motor in the cell membrane; the filament/motor structure is called a flagellum. The energy for rotation comes from the membrane iron gradient. Like any rotary motor, the bacterial flagellar motor possesses a stator (the non-rotating part) and a rotor (the rotating part). FliG, FliN, and FliM are three proteins that function in a complex on the rotor. Recently, x-ray crystallography has been used to determine the three-dimensional structure of a domain of the rotor protein FliG. This domain functions

directly in motor rotation, and is known to interact with proteins of the stator. This is the first high-resolution structure determined for any component of the flagellum. In the work proposed here, the FliG domain structure will be exploited to guide detailed biochemical and functional studies of this key rotor component. Another flagellar rotor protein, FliN, has also been crystallized and preliminary data show that it will be feasible to determine its structure. The structure of FliN will be determined, and also used to guide biochemical and functional studies. The long-term goal of this work is to understand the structure of the protein complex that forms the flagellar rotor, and to understand the mechanism of motor rotation in light of this structure. The proposed work will bring us significantly nearer this goal, by revealing structures and spatial relationship of rotor components in unprecedented detail.

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

- **Project Title: SUBSTANCE P IN PATHOGENESIS OF CRYPTOSPORIDIOSIS IN AIDS**

  Principal Investigator & Institution: Robinson, Prema; Medicine; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2003; Project Start 05-JUN-2003; Project End 31-MAY-2005

  Summary: (provided by applicant): Cryptosporidiosis, caused by the protozoan parasite, Cryptosporidium parvum, is self-limited in normal hosts but can cause life threatening, chronic **diarrhea** in AIDS patients. No safe and effective treatment has been successfully developed for cryptospofidiosis associated with advanced AIDS. C. parvum infection causes intestinal physiologic changes like, increased chloride anion secretion (CI) and epithelial barrier disruption that leads to watery **diarrhea.** Substance P (SP), a neuropeptide, is a pain transmitter and can cause C1- ion secretion in human intestinal explants. We have previously studied SP expression in jejunal biopsies of AIDS patients with natural severe cryptosporidiosis and normal volunteers experimentally challenged with C. parvum (mild disease). SP expression was stronger in AIDS patients compared to normal volunteers with mild self-limited cryptosporidiosis. We hypothesize that SP is a key mediator of chronic intestinal symptoms in AIDS associated cryptosporidiosis. We also hypothesize that SP expression will be elevated in intestinal tissues of immunodeficient hosts because of cryptosporidiosis infection, HIV infection alone will not cause increased SP expression. To verify these hypotheses, we propose to use an immunodeficient animal model of cryptosporidiosis, ie. primates with AIDS (after experimental SIV infection) and cryptosporidiosis as an opportunistic naturally occurring infection. Advantage of an animal model is that, it is easier to procure large tissue samples from an animal model to that from AIDS patients with cryptosporidiosis, and, studies aimed at defining molecular targets responsible for disease pathogenesis and initial therapeutic testing of specific antagonists can best be studied using animal derived tissues. The goal of this project is to test the hypothesis that SP mediates severe symptoms of cryptosporidiosis in immunodeficient hosts. Specific aim 1: To determine if intestinal SP is upregulated in immunodeficient animals with chronic naturally infected cryptosporidiosis as compared to immunodeficient animals without cryptosporidiosis or normal immunocompetent macaques with subclinical experimental cryptosporidiosis. Ileal expression of SP mRNA and protein levels will be compared between immunodeficient macaques (with AIDS) with and without naturally occurring C. parvum infection and in normal macaques with and without subclinical experimental C. parvum infection. Specific aim 2: To test the hypothesis that SP is a key factor that mediates intestinal physiological alterations that lead to watery **diarrhea** in naturally occurring chronic cryptosporidiosis associated with immunodeficient hosts. C1- ion

secretion and barrier integrity will be compared between ileal tissues from SIV infected macaques (with AIDS) with and without naturally occurring C. parvum infection in the presence and absence of SP receptor antagonist by the Ussing chamber technique. These studies will determine the role of SP in the pathogenesis of C. parvum induced **diarrhea.** Evidence implicating SP in the disease process would support the use of SP receptor antagonists as a therapy for the life threatening illness associated with AIDS related cryptosporidiosis and perhaps other intestinal pathogens.

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

- **Project Title: SURVEILLANCE OF HUMAN CALICIVIRUS IN CHINA**

  Principal Investigator & Institution: Jiang, Xi; Associated Professor; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

  Timing: Fiscal Year 2001; Project Start 01-JUN-2000; Project End 31-MAY-2003

  Summary: Acute infectious gastroenteritis is one of the most important diseases in China. Based on a nationwide surveillance of 21 provinces in 1988, there were 863 million diarrheal episodes per year in China, of which 290 million occurred in children under 5 years of age. Limited studies on human calicivirus (HuCV)-associated gastroenteritis have been performed in developing countries, including China. The hypotheses of this study are that HuCVs play an important role in acute gastroenteritis in children and adults in China and that new HuCV strains with genetic and antigenic properties distinct from currently known strains exist. These hypotheses will be fulfilled by the following specific aims: 1. To determine the role of HuCVs as a cause of severe **diarrhea** in children and of outbreaks of acute gastroenteritis in the general population by a nationwide surveillance in ten cities and one rural area in China. 2. To determine genetic variation of epidemic strains of HuCVs by cloning and sequencing strains detected in stool specimens from the surveys as well as from historic collections of stool specimens from children. 3. To extend understanding of the genetic variation of HuCVs by cloning the entire capsid gene of newly discovered strains and to develop EIAs by expression of the viral capsid protein in baculovirus.

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

- **Project Title: TRANSMISSION OF H. PYLORI INFECTION IN THE RHESUS MONKEY**

  Principal Investigator & Institution: Solnick, Jay V.; Associate Professor of Medicine; Internal Medicine; University of California Davis Sponsored Programs, 118 Everson Hall Davis, Ca 95616

  Timing: Fiscal Year 2001; Project Start 12-SEP-2001; Project End 31-AUG-2006

  Summary: (provided by the applicant): Infection with Helicobacter pylori causes a histological gastritis that in some individuals is associated with the development of peptic ulcer disease or gastric malignancy. Although H. pylori may be the most common human bacterial infection, the mechanism by which it is transmitted remains unknown. Person to person transmission probably accounts for most infections. Yet one of the great paradoxes in the epidemiology of H. pylori is that when one examines the gastric lining, the bacterium is ubiquitous, but when fecal or oral secretions are studied it is often difficult to find. This may reflect the difficulty of studying in humans the role of acuity of infection, age of the host, and the possible effects of vomiting, **diarrhea,** and the CagA pathogenicity island on transmission. Rhesus monkeys are naturally infected with H. pylori that is very similar to strains that infect humans, and this animal model provides a unique opportunity to study experimentally the transmission of H. pylori in

a naturally infected host. We hypothesize that acuity of infection, the presence of vomiting and **diarrhea,** and the CagA pathogenicity island are critical variables in transmission of H. pylori. Furthermore, we propose that there may be a cooperativity between transmission of H. pylori and transmission of bacterial enteric diseases. Diarrheal and vomiting diseases may increase H. pylori transmission by increasing the shedding H. pylori in feces and vomitus, and in turn, H. pylori infection may cause increased gastric pH and thereby promote infection with enteric bacteria by reducing the gastric bactericidal barrier. We propose to address four specific aims in this proposal: l) Determine how H. pylori is shed into the environment during acute and chronic infection; 2) Examine experimentally the effects of vomiting, **diarrhea** and the CagA pathogenicity island on the natural transmission of H. pylori; 3) Determine the effects of H. pylori infection on the acquisition of Campylobacter jejuni; and 4) Determine the effects of the CagA pathogenicity island on colonization and shedding.

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

- **Project Title: TRANSPORT AND LIPID INTERACTIONS OF A NOVEL ENTEROTOXIN**

  Principal Investigator & Institution: Ball, Judith M.; Veterinary Pathobiology; Texas A&M University System College Station, Tx 778433578

  Timing: Fiscal Year 2001; Project Start 01-JUN-2001; Project End 31-MAY-2006

  Summary: (provided by applicant): Rotaviruses cause severe, life-threatening diarrheal disease in young children resulting in over a million deaths worldwide. In 1996, we identified the first viral enterotoxin, rotavirus NSP4, and introduced a new mechanism of rotavirus-induced **diarrhea.** NSP4-induced **diarrhea** is mediated by a phophoinositide signal transduction pathway that results in inositol triphosphate production, increased intracellular calcium, and chloride secretion. Yet, discrete lipid interactions and intracellular targeting of NSP4 in mammalian cells are unknown. Nor have structural studies been completed with defined model membranes. Our goals to define the intracellular transport and discrete cholesterol- and caveolin-1-interacting domains of NSP4 will be accomplished by combining innovative biophysical measurements, laser imaging, fluorescent spectroscopy and resonance energy transfer studies, with classical genetic and biochemical techniques. Our hypothesis is the enterotoxin-containing, cytoplasmic domain of NSP4 (cNSP4) is cleaved from the ER, transported to the cell surface in association with caveolin-1 and/or caveolar vesicles, and targeted to plasma membrane caveolae to interact with the signaling machinery of the cell. Our preliminary data show NSP4 and its active peptide, NSP4114-135, preferentially bind highly curved, anionic, cholesterol-rich membrane vesicles that mimic the plasma membrane microdomain, caveolae. Moreover, a cytoplasmic, C-terminal region of NSP4 is released from the ER when expressed in mammalian cells. We have shown cNSP4 colocalizes with caveolin-1, verifying that NSP4 and caveolin-1 are sorted to the same intracellular location. We now propose an in depth study of the mechanism of NSP4 transport in intestinal cells. The specific aims are to: 1. Characterize the intracellular location of the cleaved NSP4 fragment (cNSP4) and cNSP4-caveolin-1 interaction(s) in mammalian cells. 2. Determine the role of caveolin-1/caveolae in the intracellular transport of cNSP4. 3. Delineate the domains of NSP4 that influence cNSP4 transport in mammalian cells. This investigation will contribute new insights into our understanding of the newly discovered plasma membrane microdomains (such as caveolae); broaden our knowledge of intracellular protein-membrane/lipid interactions; contribute to our understanding of enterotoxin function; and disclose basic intracellular

processes whereby othcr toxins may interact with the cell. Further, this study may reveal new intracellular protein transport pathways.

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- **Project Title: TRIAL OF VITAMINS AMONG CHILDREN OF HIV-INFECTED MOTHERS**

  Principal Investigator & Institution: Fawzi, Wafaie W.; Associate Professor; Nutrition; Harvard University (Sch of Public Hlth) Public Health Campus Boston, Ma 02460

  Timing: Fiscal Year 2003; Project Start 09-JUN-2003; Project End 31-MAY-2008

  Summary: (provided by applicant): An increasing body of evidence supports the efficacy of single and, more recently, multiple micronutrient supplementation in reducing morbidity and mortality in susceptible populations. For example, we have recently completed a multiple micronutrient supplementation trial in HIV-positive Tanzanian women that showed a significant reduction in pre-term birth, fetal loss, and low birthweight. In children, we and others have shown the beneficial effects of vitamin A supplementation in reducing diarrheal disease and mortality. Our next priority is to evaluate the efficacy of multiple micronutrient supplementation in susceptible children. Children born to HIV-infected women are at risk of multiple micronutrient deficiencies due to poor dietary intake, malabsorption, and increased metabolic needs. In addition, these children, if infected with HIV themselves, are at significantly higher risk of death due to infectious illnesses than their non-infected peers. In this application, we propose to study the efficacy of micronutrient supplementation in reducing the risk of death and other adverse health outcomes among infants and young children born to HIV-positive Tanzanian women. Infants will be recruited and randomly assigned to either micronutrients or a placebo liquid given daily. The primary outcome will be mortality. Secondary outcomes will include occurrence of **diarrhea,** occurrence of respiratory tract infection, weight and length gain, and HIV transmission. A subset of infants will undergo evaluation of intestinal permeability and biochemical nutritional assessment. The study will be carried out as a collaborative effort between the Harvard School of Public Health and Muhimbili University College of Health Sciences, Dar-es-Salaam, Tanzania.

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

- **Project Title: UTILITY OF MUSCARINIC AGONISTS FOR ALZHEIMER'S DISEASE**

  Principal Investigator & Institution: Ghosh, Debasis; Cognitive Pharmaceuticals, Ltd 333 14Th St Toledo, Oh 43624

  Timing: Fiscal Year 2002; Project Start 01-MAY-2002; Project End 31-OCT-2003

  Summary: (provided by applicant): The purpose of the present study is to assess the utility of muscarinic agonists in treating Alzheimer's disease. Levels of acetylcholine decrease in Alzheimer's disease, resulting in memory deficits. Efforts to treat Alzheimer's disease have been based on compounds that mimic acetylcholine without producing side effects such as salivation or **diarrhea.** Unfortunately, muscarinic agonists have shown limited clinical utility due to low efficacy, poor selectivity or high toxicity. Recent studies suggest however, that muscarinic agonists might be useful in treating not only memory impairments, but also the underlying causes of Alzheimer's disease. In particular, muscarinic agonists promote a-secretase activity, thereby limiting the production of b-amyloid, and stimulate Akt , which prevents the phosphorylation of tau proteins. Thus administration of efficacious, selective and safe muscarinic agonists could

be beneficial in the early stages of Alzheimer's disease. 5-(3-Ethyl-1,2 4-oxadiazol-5-yl)-1 ,4,5,6-tetrahydropyrimidine (CDD-0 102) activates muscarinic receptors in brain and improves memory function with few side effects and low toxicity in the present study, CDD-01 02 will be examined for its ability to promote a-secretase and Akt activity. Metabolites of CDD-0102 will be determined and examined for receptor activity to assess safety. Together, the studies will assess the utility of CDD-01 02 in treating not only cognitive and memory deficits, but also the progression of Alzheimer's disease.

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

- **Project Title: VIRULENCE IN ENTEROAGGREGATIVE E COLI**

  Principal Investigator & Institution: Nataro, James P.; Professor; Pediatrics; University of Maryland Balt Prof School Baltimore, Md 21201

  Timing: Fiscal Year 2001; Project Start 01-AUG-2000; Project End 31-JUL-2005

  Summary: Enteroaggregative Escherichia coli (EAEC) is an increasingly recognized pathogen of human **diarrhea.** This organism has been implicated in sporadic **diarrhea** in developing and industrialized countries, in the persistent **diarrhea** syndrome in AIDS patients and children in the developing world, in traveler's **diarrhea,** and in various diarrheal outbreaks. The PI discovered this pathotype of diarrheagenic E. coli and has been the leader in describing the pathogenesis and epidemiology of this organism, This is a competing continuation of our fundamental work on the pathogenesis of EAEC infection. Overall, our objectives are to advance knowledge of EAEC pathogenesis, to better define true EAEC pathogens, to refine diagnostic methods and to identify protective immunogen. The three aims of this proposal seek to extend the most important and promising aspects of the work funded under the current award. Aim 1: Characterization of EAEC adhesion-Aggregation is the defining characterization of EAEC. Our observations suggest that aggregative adherence (AA) is a prelude to biofilm formation, which occurs in vivo and which can be modeled in vitro. In this aim, we will further elucidate fundamental aspects of EAEC adherence. Aim 2: The Regulation of EAEC virulence- AggR is a highly prevalent and conserved activator of AAF expression. However, nothing else is known of the regulation of EAEC virulence. Beginning with AggR, we will expand our studies of EAEC gene regulation. Aim 3: Reconstructing EAEC-We will use in vitro organ culture and T84 cell models of EAEC infection to answer the question: what genes are necessary and sufficient to confer the effects that we observe? The work under this award will greatly advance the current state of knowledge of EAEC and will result in the identification of pathogenetic mechanisms, of diagnostic reagents and in vaccine candidates.

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

- **Project Title: VITAMIN A/ZINC--PREVENTION OF PNEUMONIA (VAZPOP) STUDY**

  Principal Investigator & Institution: Griffiths, Jeffrey K.; Associate Professor; Family Medicine & Cmty Health; Tufts University Boston Boston, Ma 02111

  Timing: Fiscal Year 2001; Project Start 18-JAN-2000; Project End 31-DEC-2004

  Summary: (Adapted from applicant's description): The Vitamin A and Zinc - Prevention of Pneumonia (VAZPOP) Study. Linking Vitamin A and Zinc Deficiencies, Immunity, Growth, and the Prevention of the Leading Cause of Childhood Death. The objective is to delineate how vitamin A and zinc supplementation interact in improving immunity, fostering growth, and preventing infection, in populations at risk for malnutrition and vitamin A and zinc deficiency. Malnutrition is involved in half of the global deaths in

children less than 5. Acute respiratory infection (ARI), especially acute lower respiratory infection (ALRI) or pneumonia, is the leading cause of death in children. The investigators propose to conduct a randomized, placebo controlled, double blind, nutritionally stratified study of low dose vitamin A, 10 mg/day elemental zinc, both, or placebo in 2,400 children in Quito Ecuador. They will test the hypotheses that: a) low-dose vitamin A has paradoxically positive and negative effects on ALRI in underweight and well nourished children; b) zinc will protect against ALRI and **diarrhea** while boosting cell mediated immunity; c) growth will be fostered by zinc (and potentially by vitamin A) in deficient children; and d) misclassification of ALRI cases can mask the benefits or risks of vitamin A. The investigators will use state-of- the-art field techniques to assess body composition and growth, and utilize sophisticated techniques to assess vitamin A and zinc deficiency. In addition, they will use rigorous definitions of ALRI/pneumoma to avoid misclassification and ascertainment bias, which may have affected prior studies.

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

E-Journals: PubMed Central[3]

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

- **A Localized Adherence-Like Pattern as a Second Pattern of Adherence of Classic Enteropathogenic Escherichia coli to HEp-2 Cells That Is Associated with Infantile Diarrhea.** by Scaletsky IC, Pedroso MZ, Oliva CA, Carvalho RL, Morais MB, Fagundes-Neto U.; 1999 Jul;
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- **A Stem-Loop Motif Formed by the Immediate 5[prime prime or minute] Terminus of the Bovine Viral Diarrhea Virus Genome Modulates Translation as well as Replication of the Viral RNA.** by Yu H, Isken O, Grassmann CW, Behrens SE.; 2000 Jul 1;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=112077
- **Adherence Patterns and Adherence-Related DNA Sequences in Escherichia coli Isolates from Children with and without Diarrhea in Sao Paulo City, Brazil.** by Gomes TA, Vieira MA, Abe CM, Rodrigues D, Griffin PM, Ramos SR.; 1998 Dec;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=105249

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

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

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

- **Age-specific prevalence of Escherichia coli with localized and aggregative adherence in Venezuelan infants with acute diarrhea.** by Gonzalez R, Diaz C, Marino M, Cloralt R, Pequeneze M, Perez-Schael I.; 1997 May; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=232711
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- **Analysis of incidence of infection with enterotoxigenic Escherichia coli in a prospective cohort study of infant diarrhea in Nicaragua.** by Paniagua M, Espinoza F, Ringman M, Reizenstein E, Svennerholm AM, Hallander H.; 1997 Jun; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=229758
- **Antibacterial Activity Evaluation of Microcin J25 against Diarrheagenic Escherichia coli.** by Sable S, Pons AM, Gendron-Gaillard S, Cottenceau G.; 2000 Oct; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=92352
- **Antimicrobial Resistance of Diarrheagenic Escherichia coli Isolated from Children under the Age of 5 Years from Ifakara, Tanzania.** by Vila J, Vargas M, Casals C, Urassa H, Mshinda H, Schellemberg D, Gascon J.; 1999 Dec; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=89608
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- **Antiviral Effect of N-Butyldeoxynojirimycin against Bovine Viral Diarrhea Virus Correlates with Misfolding of E2 Envelope Proteins and Impairment of Their Association into E1-E2 Heterodimers.** by Branza-Nichita N, Durantel D, Carrouee-Durantel S, Dwek RA, Zitzmann N.; 2001 Apr 15; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=114844
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The National Library of Medicine: PubMed

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

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

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

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  Source: Paediatric Drugs. 2003; 5(3): 151-65. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12608880&dopt=Abstract

- **Two- to three-fold increase in blood tacrolimus (FK506) levels during diarrhea in liver-transplanted children.**
  Author(s): Berengue JI, Lopez-Espinosa JA, Ortega-Lopez J, Sanchez-Sanchez L, Castilla-Valdes P, Asensio-Llorente M, Margarit-Creixell C.
  Source: Clinical Transplantation. 2003 June; 17(3): 249-53.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12780676&dopt=Abstract

- **Underlying disease severity as a major risk factor for nosocomial Clostridium difficile diarrhea.**
  Author(s): Kyne L, Sougioultzis S, McFarland LV, Kelly CP.
  Source: Infection Control and Hospital Epidemiology : the Official Journal of the Society of Hospital Epidemiologists of America. 2002 November; 23(11): 653-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12452292&dopt=Abstract

- **Virulence markers of enteroaggregative Escherichia coli isolated from children and adults with diarrhea in Brasilia, Brazil.**
  Author(s): Piva IC, Pereira AL, Ferraz LR, Silva RS, Vieira AC, Blanco JE, Blanco M, Blanco J, Giugliano LG.
  Source: Journal of Clinical Microbiology. 2003 May; 41(5): 1827-32.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12734212&dopt=Abstract

- **Virus diversity in a winter epidemic of acute diarrhea in France.**
  Author(s): Chikhi-Brachet R, Bon F, Toubiana L, Pothier P, Nicolas JC, Flahault A, Kohli E.
  Source: Journal of Clinical Microbiology. 2002 November; 40(11): 4266-72.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12409408&dopt=Abstract

- **Vitamin A supplementation and childhood morbidity from diarrhea and respiratory infections: a meta-analysis.**
  Author(s): Grotto I, Mimouni M, Gdalevich M, Mimouni D.
  Source: The Journal of Pediatrics. 2003 March; 142(3): 297-304.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12640379&dopt=Abstract

- **What's new on defining diarrhea in tube-feeding studies?**
  Author(s): Lebak KJ, Bliss DZ, Savik K, Patten-Marsh KM.
  Source: Clinical Nursing Research. 2003 May; 12(2): 174-204. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12741669&dopt=Abstract

CHAPTER 2. NUTRITION AND DIARRHEA

Overview

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

Finding Nutrition Studies on Diarrhea

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

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

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

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

The following is a typical result when searching for recently indexed consumer information on diarrhea:

- **A rice-based diet with green banana or pectin reduced diarrhea in infants better than a rice-alone diet.**
  Author(s): Family Practice Residency Program, Eastern Maine Medical Center, Bangor, Mainw, USA.
  Source: Triplehorn, Clay Millard, Peter S ACP-J-Club. 2002 Mar-April; 136(2): 67 1056-8751
- **Acarbose related diarrhea: increased butyrate upregulates prostaglandin E.**
  Author(s): Department of Psychiatry, College of Medicine, University of Vermont, Burlington 05401, USA. rekast@email.com
  Source: Kast, R E Inflamm-Res. 2002 March; 51(3): 117-8 1023-3830
- **An overview of diarrhea in the patient receiving enteral nutrition.**
  Author(s): Continuing Education, Practice and Research, Indianapolis, Indiana 46219, USA. P.Eisenberg@ehealthindiana.com
  Source: Eisenberg, Patti Gastroenterol-Nurs. 2002 May-June; 25(3): 95-104 1042-895X
- **Campylobacter-induced enteritis and diarrhea in captive cotton-top tamarins (Saguinus oedipus) during the first year of life.**
  Source: Johnson, L.D. Ausman, L.M. Rolland, R.M. Chalifoux, L.V. Russell, R.G. Comp-med. Memphis, TN : American Association for Laboratory Animal Science, 2000-. June 2001. volume 51 (3) page 257-261. 1532-0820
- **Can yogurt reduce diarrhea caused by antibiotics.**
  Source: Tufts-Univ-health-nutr-lett. New York, NY : Tufts University Health & Nutrition Letter, c1997-. January 2000. volume 17 (11) page 3.
- **Drug prophylaxis for travelers' diarrhea.**
  Author(s): Department of Specific Prophylaxis and Tropical Medicine, Institute of Pathophysiology, University of Vienna, A-1095 Vienna, Austria.
  Source: Rendi Wagner, Pamela Kollaritsch, Herwig Clin-Infect-Dis. 2002 March 1; 34(5): 628-33 1537-6591
- **Estrogen replacement in a protein S deficient patient leads to diarrhea, hyperglucagonemia, and osteonecrosis.**
  Author(s): Cholesterol Center, Jewish Hospital, Cincinnati, Ohio 45229, USA. glueckch@healthall.com
  Source: Glueck, C J Phillips, H G Cameron, D Wang, P JOPage 2001 September; 2(5): 323-9 1590-8577
- **Evaluation of anti-diarrheal activity of Cleome viscosa L. extract in rats.**
  Author(s): Division of Pharmacognosy, Department of Pharmaceutical Technology, Faculty of Engineering & Technology, Jadavpur University, Calcutta, India.
  Source: Devi, B P Boominathan, R Mandal, S C Phytomedicine. 2002 December; 9(8): 739-42 0944-7113
- **Experimental effects of Saccharomyces boulardii on diarrheal pathogens.**
  Author(s): Laboratoire de gastroenterologie et nutrition, universite de Nice-Sophia-Antipolis, faculte de medecine, 28 avenue de Valombrose, 06107 Nice cedex 2, France. czerucka@unice.fr
  Source: Czerucka, Dorota Rampal, Patrick Microbes-Infect. 2002 June; 4(7): 733-9 1286-4579

- **Intractable diarrhea in hyperthyroidism: management with beta-adrenergic blockade.**
  Author(s): Department of Internal Medicine, Kalamazoo Center for Medical Studies, Michigan State University School of Medicine, 49008, USA.
  Source: Bricker, L A Such, F Loehrke, M E Kavanaugh, K Endocr-Pract. 2001 Jan-February; 7(1): 28-31 1530-891X

- **Microbicidal effect of medicinal plant extracts (Psidium guajava Linn. and Carica papaya Linn.) upon bacteria isolated from fish muscle and known to induce diarrhea in children.**
  Author(s): Instituto de Ciencias do Mar, Universidade Federal do Ceara, Ceara, Brasil. regpoema@labomar.ufc.br
  Source: Vieira, R H Rodrigues, D P Goncalves, F A Menezes, F G Aragao, J S Sousa, O V Rev-Inst-Med-Trop-Sao-Paulo. 2001 May-June; 43(3): 145-8 0036-4665

- **Pharmacological studies on Myristica fragrans--antidiarrheal, hypnotic, analgesic and hemodynamic (blood pressure) parameters.**
  Author(s): Department of Pharmacology, All India Institute of Medical Sciences, New Delhi, India. jkgrover@hotmail.com
  Source: Grover, J K Khandkar, S Vats, V Dhunnoo, Y Das, D Methods-Find-Exp-Clin-Pharmacol. 2002 December; 24(10): 675-80 0379-0355

- **Prevention of antibiotic-associated diarrhea in infants by probiotics.**
  Author(s): Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.
  Source: Jirapinyo, P Densupsoontorn, N Thamonsiri, N Wongarn, R J-Med-Assoc-Thai. 2002 August; 85 Suppl 2: S739-42 0125-2208

- **Risk and prognostic factors for diarrheal disease in Brazilian infants: a special case-control design application.**
  Author(s): Departamento de Medicina Social, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, 90035-003, Brasil. scfuchs@zaz.com.br
  Source: Fuchs, S C Victora, C G Cad-Saude-Publica. 2002 May-June; 18(3): 773-82 0102-311X

- **Testing control of radiation-induced diarrhea with a psyllium bulking agent: a pilot study.**
  Author(s): Ottawa Hospital-General Campus, Ottawa, Ontario.
  Source: Murphy, J Stacey, D Crook, J Thompson, B Panetta, D Can-Oncol-Nurs-J. 2000 Summer; 10(3): 96-100 1181-912X

- **The treatment of acute diarrhea in the third millennium: a pediatrician's perspective.**
  Author(s): Department of Pediatrics, University of Chicago, 5841 S. Maryland Ave., Chicago, IL 60637, USA. sguandal@peds.bsd.uchicago.edu
  Source: Guandalini, Stefano Acta-Gastroenterol-Belg. 2002 Jan-March; 65(1): 33-6 0001-5644

- **Untractable diarrhea due to late onset celiac disease of the adult following pancreatoduodenectomy.**
  Author(s): Division of General Surgery and Transplants, Department of Oncology, Transplants and New Technologies in Medicine, University of Pisa, 56124 Pisa, Italy. u.boggi@patchir.med.unipi.it
  Source: Boggi, U Bellini, R Rossetti, E Pietrabissa, A Mosca, F Hepatogastroenterology. 2001 Jul-August; 48(40): 1030-2 0172-6390

- **Zinc or vitamin A reduced diarrhea in young, poor Bangladeshi children.**
  Author(s): Tamil Nadu Dr. M.G.R. Medial University, Chennai, Tamil Nadau, India.

Source: Datta, Manjula ACP-J-Club. 2002 Mar-April; 136(2): 66 1056-8751

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

- **A rice-based diet with green banana or pectin reduced diarrhea in infants better than a rice-alone diet.**
  Author(s): Family Practice Residency Program, Eastern Maine Medical Center, Bangor, Mainw, USA.
  Source: Triplehorn, Clay Millard, Peter S ACP-J-Club. 2002 Mar-April; 136(2): 67 1056-8751

- **Acarbose related diarrhea: increased butyrate upregulates prostaglandin E.**
  Author(s): Department of Psychiatry, College of Medicine, University of Vermont, Burlington 05401, USA. rekast@email.com
  Source: Kast, R E Inflamm-Res. 2002 March; 51(3): 117-8 1023-3830

- **An overview of diarrhea in the patient receiving enteral nutrition.**
  Author(s): Continuing Education, Practice and Research, Indianapolis, Indiana 46219, USA. P.Eisenberg@ehealthindiana.com
  Source: Eisenberg, Patti Gastroenterol-Nurs. 2002 May-June; 25(3): 95-104 1042-895X

- **Campylobacter-induced enteritis and diarrhea in captive cotton-top tamarins (Saguinus oedipus) during the first year of life.**
  Source: Johnson, L.D. Ausman, L.M. Rolland, R.M. Chalifoux, L.V. Russell, R.G. Comp-med. Memphis, TN : American Association for Laboratory Animal Science, 2000-. June 2001. volume 51 (3) page 257-261. 1532-0820

- **Can yogurt reduce diarrhea caused by antibiotics.**
  Source: Tufts-Univ-health-nutr-lett. New York, NY : Tufts University Health & Nutrition Letter, c1997-. January 2000. volume 17 (11) page 3.

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  Author(s): Department of Specific Prophylaxis and Tropical Medicine, Institute of Pathophysiology, University of Vienna, A-1095 Vienna, Austria.
  Source: Rendi Wagner, Pamela Kollaritsch, Herwig Clin-Infect-Dis. 2002 March 1; 34(5): 628-33 1537-6591

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  Source: Glueck, C J Phillips, H G Cameron, D Wang, P JOPage 2001 September; 2(5): 323-9 1590-8577

- **Evaluation of anti-diarrheal activity of Cleome viscosa L. extract in rats.**
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  Source: Devi, B P Boominathan, R Mandal, S C Phytomedicine. 2002 December; 9(8): 739-42 0944-7113

- **Experimental effects of Saccharomyces boulardii on diarrheal pathogens.**
  Author(s): Laboratoire de gastroenterologie et nutrition, universite de Nice-Sophia-Antipolis, faculte de medecine, 28 avenue de Valombrose, 06107 Nice cedex 2, France. czerucka@unice.fr
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  Author(s): Department of Internal Medicine, Kalamazoo Center for Medical Studies, Michigan State University School of Medicine, 49008, USA.
  Source: Bricker, L A Such, F Loehrke, M E Kavanaugh, K Endocr-Pract. 2001 Jan-February; 7(1): 28-31 1530-891X

- **Microbicidal effect of medicinal plant extracts (Psidium guajava Linn. and Carica papaya Linn.) upon bacteria isolated from fish muscle and known to induce diarrhea in children.**
  Author(s): Instituto de Ciencias do Mar, Universidade Federal do Ceara, Ceara, Brasil. regpoema@labomar.ufc.br
  Source: Vieira, R H Rodrigues, D P Goncalves, F A Menezes, F G Aragao, J S Sousa, O V Rev-Inst-Med-Trop-Sao-Paulo. 2001 May-June; 43(3): 145-8 0036-4665

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  Author(s): Department of Pharmacology, All India Institute of Medical Sciences, New Delhi, India. jkgrover@hotmail.com
  Source: Grover, J K Khandkar, S Vats, V Dhunnoo, Y Das, D Methods-Find-Exp-Clin-Pharmacol. 2002 December; 24(10): 675-80 0379-0355

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  Source: Jirapinyo, P Densupsoontorn, N Thamonsiri, N Wongarn, R J-Med-Assoc-Thai. 2002 August; 85 Suppl 2: S739-42 0125-2208

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  Author(s): Departamento de Medicina Social, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, 90035-003, Brasil. scfuchs@zaz.com.br
  Source: Fuchs, S C Victora, C G Cad-Saude-Publica. 2002 May-June; 18(3): 773-82 0102-311X

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  Author(s): Ottawa Hospital-General Campus, Ottawa, Ontario.
  Source: Murphy, J Stacey, D Crook, J Thompson, B Panetta, D Can-Oncol-Nurs-J. 2000 Summer; 10(3): 96-100 1181-912X

- **The treatment of acute diarrhea in the third millennium: a pediatrician's perspective.**
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  Source: Guandalini, Stefano Acta-Gastroenterol-Belg. 2002 Jan-March; 65(1): 33-6 0001-5644

- **Untractable diarrhea due to late onset celiac disease of the adult following pancreatoduodenectomy.**
  Author(s): Division of General Surgery and Transplants, Department of Oncology, Transplants and New Technologies in Medicine, University of Pisa, 56124 Pisa, Italy. u.boggi@patchir.med.unipi.it
  Source: Boggi, U Bellini, R Rossetti, E Pietrabissa, A Mosca, F Hepatogastroenterology. 2001 Jul-August; 48(40): 1030-2 0172-6390

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  Author(s): Tamil Nadu Dr. M.G.R. Medial University, Chennai, Tamil Nadau, India.

Source: Datta, Manjula ACP-J-Club. 2002 Mar-April; 136(2): 66 1056-8751

Federal Resources on Nutrition

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

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

Additional Web Resources

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

- AOL: **http://search.aol.com/cat.adp?id=174&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/med_nutrition.html**
- Google: **http://directory.google.com/Top/Health/Nutrition/**
- Healthnotes: **http://www.healthnotes.com/**
- Open Directory Project: **http://dmoz.org/Health/Nutrition/**
- Yahoo.com: **http://dir.yahoo.com/Health/Nutrition/**
- WebMD®Health: **http://my.webmd.com/nutrition**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**

The following is a specific Web list relating to diarrhea; 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**

  Ascorbic Acid
  Source: Integrative Medicine Communications; www.drkoop.com

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

  Folic Acid
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,887,00.html

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

  Pantothenic Acid
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,882,00.html

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

  Vitamin B3
  Source: Healthnotes, Inc.; www.healthnotes.com

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

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

  Vitamin C
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,904,00.html

  Vitamin C (Ascorbic Acid)
  Source: Integrative Medicine Communications; www.drkoop.com

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

  Vitamin D
  Alternative names: Calciferol, Calcitrol, Cholecalciferol, Erocalciferol
  Source: Integrative Medicine Communications; www.drkoop.com

Vitamin D
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,905,00.html

Vitamin E
Alternative names: Alpha-Tocopherol, Beta-Tocopherol, D-Alpha-Tocopherol, Delta-Tocopherol, Gamma-Tocopherol
Source: Integrative Medicine Communications; www.drkoop.com

Vitamin E
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,906,00.html

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

- **Minerals**

Alpha-tocopherol
Source: Integrative Medicine Communications; www.drkoop.com

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

Beta-tocopherol
Source: Integrative Medicine Communications; www.drkoop.com

Calcium/magnesium
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,937,00.html

Carnitine (l-carnitine)
Source: Integrative Medicine Communications; www.drkoop.com

Chondroitin
Alternative names: chondroitin sulfate, sodium chondroitin sulfate
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

D-alpha-tocopherol
Source: Integrative Medicine Communications; www.drkoop.com

Delta-tocopherol
Source: Integrative Medicine Communications; www.drkoop.com

Gamma-tocopherol
Source: Integrative Medicine Communications; www.drkoop.com

L-carnitine
Source: Integrative Medicine Communications; www.drkoop.com

Lecithin and Choline
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10040,00.html

Lecithin/phosphatidylcholine/choline
Source: Healthnotes, Inc.; www.healthnotes.com

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

Magnesium
Source: Integrative Medicine Communications; www.drkoop.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

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

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

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

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

Potassium
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10086,00.html

Quercetin
Source: Integrative Medicine Communications; www.drkoop.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: Healthnotes, Inc.; www.healthnotes.com

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

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

Zinc
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10071,00.html

- **Food and Diet**

Blackberries
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/foods_view/0,1523,142,00.html

Cinnamon
Alternative names: Cinnamomum zeylanicum
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

Dairy-free Diet
Source: Healthnotes, Inc.; www.healthnotes.com

Fat Alternatives and Fat Replacers
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,786,00.html

Gluten-free Diet
Source: Healthnotes, Inc.; www.healthnotes.com

Guava
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/foods_view/0,1523,139,00.html

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

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

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

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

Milk
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/foods_view/0,1523,95,00.html

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

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

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

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

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

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

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

CHAPTER 3. ALTERNATIVE MEDICINE AND DIARRHEA

Overview

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

- **Complementary Therapies: Overview and State of the Art**

  Source: Cancer Nursing. 22(1): 85-90. February 1999.

  Summary: This journal article provides an overview of the benefits and potential problems of complementary therapies for cancer. The author distinguishes between alternative and complementary therapies, noting that alternative therapies are used instead of conventional cancer treatment, whereas complementary therapies are used as adjuncts to mainstream care. In the author's opinion, alternative therapies can be dangerous clinically and also because their use may delay patient's receipt of mainstream care. The first part of this article reviews the evidence regarding the seven categories of alternative therapies established by the Office of Alternative Medicine. The second part describes the potential benefits of selected complementary therapies for some of the difficulties associated with cancer diagnosis, treatment, and survival including therapies for stress and anxiety, constipation, depression, **diarrhea,** and nausea. The third part outlines the risks associated with certain herbal products,

including products with potentially harmful effects, products that are ineffective, products that are fake or highly contaminated, products with inaccurate labeling, and products based on unverified evidence. The article has 5 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 diarrhea 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 "diarrhea" (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 diarrhea:

- **AIDS-associated diarrhea and wasting in Northeast Brazil is associated with subtherapeutic plasma levels of antiretroviral medications and with both bovine and human subtypes of Cryptosporidium parvum.**
  Author(s): Brantley RK, Williams KR, Silva TM, Sistrom M, Thielman NM, Ward H, Lima AA, Guerrant RL.
  Source: The Brazilian Journal of Infectious Diseases : an Official Publication of the Brazilian Society of Infectious Diseases. 2003 February; 7(1): 16-22.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12807688&dopt=Abstract

- **Antibiotic-associated diarrhea.**
  Author(s): Periman P.
  Source: The New England Journal of Medicine. 2002 July 11; 347(2): 145; Author Reply 145.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12110748&dopt=Abstract

- **Antiviral activity of Petiveria alliacea against the bovine viral diarrhea virus.**
  Author(s): Ruffa MJ, Perusina M, Alfonso V, Wagner ML, Suriano M, Vicente C, Campos R, Cavallaro L.
  Source: Chemotherapy. 2002 July; 48(3): 144-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12138331&dopt=Abstract

- **Beyond ORT: a new look at diarrheal disease control.**
  Author(s): Northrup R.
  Source: Cedpa World Wide. 1988 January-March; 5(1): 5-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12281575&dopt=Abstract

- **Causes of childhood diarrhea as perceived by mothers in the Punjab, Pakistan.**
  Author(s): Nielsen M, Hoogvorst A, Konradsen F, Mudasser M, van der Hoek W.

Source: Southeast Asian J Trop Med Public Health. 2003 June; 34(2): 343-51.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12971560&dopt=Abstract

- **Clinical pharmacokinetics of irinotecan and its metabolites in relation with diarrhea.**
Author(s): Xie R, Mathijssen RH, Sparreboom A, Verweij J, Karlsson MO.
Source: Clinical Pharmacology and Therapeutics. 2002 September; 72(3): 265-75.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12235447&dopt=Abstract

- **Constipation, diarrhea, and symptomatic hemorrhoids during pregnancy.**
Author(s): Wald A.
Source: Gastroenterology Clinics of North America. 2003 March; 32(1): 309-22, Vii. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12635420&dopt=Abstract

- **Cyclooxygenase-2 inhibition with celecoxib enhances antitumor efficacy and reduces diarrhea side effect of CPT-11.**
Author(s): Trifan OC, Durham WF, Salazar VS, Horton J, Levine BD, Zweifel BS, Davis TW, Masferrer JL.
Source: Cancer Research. 2002 October 15; 62(20): 5778-84.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12384538&dopt=Abstract

- **Diarrhea and acaroid mites: a clinical study.**
Author(s): Li CP, Cui YB, Wang J, Yang QG, Tian Y.
Source: World Journal of Gastroenterology : Wjg. 2003 July; 9(7): 1621-4.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12854179&dopt=Abstract

- **Diarrhea and ARI in rural areas of Bangladesh.**
Author(s): Piechulek H, Al-Sabbir A, Mendoza-Aldana J.
Source: Southeast Asian J Trop Med Public Health. 2003 June; 34(2): 337-42.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12971559&dopt=Abstract

- **Diarrhea.**
Author(s): Hu J.
Source: J Tradit Chin Med. 2002 March; 22(1): 78-80. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11977529&dopt=Abstract

- **Dietary management of diarrhea.**
Author(s): Brown KH, Bentley ME.
Source: Mothers Child. 1989; 7(3): 1-5.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12342296&dopt=Abstract

- **Domestic poultry-raising practices in a Peruvian shantytown: implications for control of Campylobacter jejuni-associated diarrhea.**
  Author(s): Harvey SA, Winch PJ, Leontsini E, Torres Gayoso C, Lopez Romero S, Gilman RH, Oberhelman RA.
  Source: Acta Tropica. 2003 April; 86(1): 41-54.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12711102&dopt=Abstract

- **Dose-response relationship and mechanism of action of Saccharomyces boulardii in castor oil-induced diarrhea in rats.**
  Author(s): Girard P, Pansart Y, Lorette I, Gillardin JM.
  Source: Digestive Diseases and Sciences. 2003 April; 48(4): 770-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12741470&dopt=Abstract

- **Effect of acupuncture in the treatment of young pigs with induced Escherichia coli diarrhea.**
  Author(s): Park ES, Jo S, Seong JK, Nam TC, Yang IS, Choi MC, Yoon YS.
  Source: J Vet Sci. 2003 August; 4(2): 124-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14610364&dopt=Abstract

- **Effect of apitherapy in piglets with preweaning diarrhea.**
  Author(s): Choi SH, Cho SK, Kang SS, Bae CS, Bai YH, Lee SH, Pak SC.
  Source: The American Journal of Chinese Medicine. 2003; 31(2): 321-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12856871&dopt=Abstract

- **Effect of Lactobacillus strains (L. casei and L. Acidophillus Strains cerela) on bacterial overgrowth-related chronic diarrhea.**
  Author(s): Gaon D, Garmendia C, Murrielo NO, de Cucco Games A, Cerchio A, Quintas R, Gonzalez SN, Oliver G.
  Source: Medicina (B Aires). 2002; 62(2): 159-63.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12038039&dopt=Abstract

- **Effect of oral administration of tormentil root extract (Potentilla tormentilla) on rotavirus diarrhea in children: a randomized, double blind, controlled trial.**
  Author(s): Subbotina MD, Timchenko VN, Vorobyov MM, Konunova YS, Aleksandrovih YS, Shushunov S.
  Source: The Pediatric Infectious Disease Journal. 2003 August; 22(8): 706-11.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12913771&dopt=Abstract

- **Effect of probiotic Lactobacillus strains in young children hospitalized with acute diarrhea.**
  Author(s): Rosenfeldt V, Michaelsen KF, Jakobsen M, Larsen CN, Moller PL, Pedersen P, Tvede M, Weyrehter H, Valerius NH, Paerregaard A.

Source: The Pediatric Infectious Disease Journal. 2002 May; 21(5): 411-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12150178&dopt=Abstract

- **Effect of probiotic Lactobacillus strains on acute diarrhea in a cohort of nonhospitalized children attending day-care centers.**
  Author(s): Rosenfeldt V, Michaelsen KF, Jakobsen M, Larsen CN, Moller PL, Tvede M, Weyrehter H, Valerius NH, Paerregaard A.
  Source: The Pediatric Infectious Disease Journal. 2002 May; 21(5): 417-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12150179&dopt=Abstract

- **Efficacy of probiotic use in acute diarrhea in children: a meta-analysis.**
  Author(s): Huang JS, Bousvaros A, Lee JW, Diaz A, Davidson EJ.
  Source: Digestive Diseases and Sciences. 2002 November; 47(11): 2625-34.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12452406&dopt=Abstract

- **Efficacy of zinc supplementation on the severity and duration of diarrhea in malnourished Turkish children.**
  Author(s): Polat TB, Uysalol M, Cetinkaya F.
  Source: Pediatrics International : Official Journal of the Japan Pediatric Society. 2003 October; 45(5): 555-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14521531&dopt=Abstract

- **Evaluation of anti-diarrheal activity of Cleome viscosa L. extract in rats.**
  Author(s): Devi BP, Boominathan R, Mandal SC.
  Source: Phytomedicine : International Journal of Phytotherapy and Phytopharmacology. 2002 December; 9(8): 739-42.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12587696&dopt=Abstract

- **Experimental effects of Saccharomyces boulardii on diarrheal pathogens.**
  Author(s): Czerucka D, Rampal P.
  Source: Microbes and Infection / Institut Pasteur. 2002 June; 4(7): 733-9. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12067833&dopt=Abstract

- **Homeopathy for childhood diarrhea: combined results and metaanalysis from three randomized, controlled clinical trials.**
  Author(s): Jacobs J, Jonas WB, Jimenez-Perez M, Crothers D.
  Source: The Pediatric Infectious Disease Journal. 2003 March; 22(3): 229-34.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12634583&dopt=Abstract

- **Hyperbaric oxygen treatment for intractable diarrhea caused by pneumatosis coli.**
  Author(s): Lustberg AM, Fantry GT, Cotto-Cumba C, Drachenberg C, Darwin PE.

Source: Gastrointestinal Endoscopy. 2002 December; 56(6): 935-7.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12447319&dopt=Abstract

- **Lactobacillus therapy for acute infectious diarrhea in children: a meta-analysis.**
Author(s): Van Niel CW, Feudtner C, Garrison MM, Christakis DA.
Source: Pediatrics. 2002 April; 109(4): 678-84.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11927715&dopt=Abstract

- **L-glutamine supplementation improves nelfinavir-associated diarrhea in HIV-infected individuals.**
Author(s): Huffman FG, Walgren ME.
Source: Hiv Clinical Trials. 2003 September-October; 4(5): 324-9.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14583848&dopt=Abstract

- **Limitations of probiotic therapy in acute, severe dehydrating diarrhea.**
Author(s): Costa-Ribeiro H, Ribeiro TC, Mattos AP, Valois SS, Neri DA, Almeida P, Cerqueira CM, Ramos E, Young RJ, Vanderhoof JA.
Source: Journal of Pediatric Gastroenterology and Nutrition. 2003 January; 36(1): 112-5.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12500005&dopt=Abstract

- **Managing nausea, vomiting, and diarrhea.**
Author(s): Highleyman L.
Source: Beta. 2002 Spring; 15(2): 29-39. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12064304&dopt=Abstract

- **Multiple-dose escalation, safety, and tolerability study of wood creosote, the principal active ingredient of seirogan, an herbal antidiarrheal medication, in healthy subjects.**
Author(s): Kuge T, Shibata T, Willett MS.
Source: Journal of Clinical Pharmacology. 2003 March; 43(3): 284-90.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12638397&dopt=Abstract

- **New diarrhea treatment available for sale as dietary supplement.**
Author(s): Gaylord G.
Source: Posit Living. 1999 September; 8(8): 18. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12510635&dopt=Abstract

- **Pharmacological studies on Myristica fragrans--antidiarrheal, hypnotic, analgesic and hemodynamic (blood pressure) parameters.**
Author(s): Grover JK, Khandkar S, Vats V, Dhunnoo Y, Das D.

Source: Methods Find Exp Clin Pharmacol. 2002 December; 24(10): 675-80.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12616960&dopt=Abstract

- **Prevention of antibiotic-associated diarrhea in children by Clostridium butyricum MIYAIRI.**
  Author(s): Seki H, Shiohara M, Matsumura T, Miyagawa N, Tanaka M, Komiyama A, Kurata S.
  Source: Pediatrics International : Official Journal of the Japan Pediatric Society. 2003 February; 45(1): 86-90.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12654076&dopt=Abstract

- **Prevention of antibiotic-associated diarrhea in infants by probiotics.**
  Author(s): Jirapinyo P, Densupsoontorn N, Thamonsiri N, Wongarn R.
  Source: J Med Assoc Thai. 2002 August; 85 Suppl 2: S739-42.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12403254&dopt=Abstract

- **Prevention of radiation-induced diarrhea with the use of VSL#3, a new high-potency probiotic preparation.**
  Author(s): Delia P, Sansotta G, Donato V, Messina G, Frosina P, Pergolizzi S, De Renzis C, Famularo G.
  Source: The American Journal of Gastroenterology. 2002 August; 97(8): 2150-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12190202&dopt=Abstract

- **Preventive effect of Kampo medicine (Hangeshashin-to) against irinotecan-induced diarrhea in advanced non-small-cell lung cancer.**
  Author(s): Mori K, Kondo T, Kamiyama Y, Kano Y, Tominaga K.
  Source: Cancer Chemotherapy and Pharmacology. 2003 May; 51(5): 403-6. Epub 2003 April 09.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12687289&dopt=Abstract

- **Probiotics use decreases antibiotic-associated diarrhea.**
  Author(s): Shaughnessy A.
  Source: American Family Physician. 2003 April 15; 67(8): 1782.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12725460&dopt=Abstract

- **Role of food antigen elimination in treating children with persistent diarrhea and malnutrition in Zambia.**
  Author(s): Amadi B.
  Source: Journal of Pediatric Gastroenterology and Nutrition. 2002 May-June; 34 Suppl 1: S54-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12082390&dopt=Abstract

- **Substantial reduction in severe diarrheal morbidity by daily zinc supplementation in young north Indian children.**
  Author(s): Bhandari N, Bahl R, Taneja S, Strand T, Molbak K, Ulvik RJ, Sommerfelt H, Bhan MK.
  Source: Pediatrics. 2002 June; 109(6): E86.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12042580&dopt=Abstract

- **Testing strategies to reduce diarrhea in persons with HIV using traditional Chinese medicine: acupuncture and moxibustion.**
  Author(s): Anastasi JK, McMahon DJ.
  Source: The Journal of the Association of Nurses in Aids Care : Janac. 2003 May-June; 14(3): 28-40.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12800810&dopt=Abstract

- **Thalidomide and irinotecan-associated diarrhea.**
  Author(s): Tchekmedyian NS.
  Source: American Journal of Clinical Oncology : the Official Publication of the American Radium Society. 2002 June; 25(3): 324.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12040298&dopt=Abstract

- **The treatment of acute diarrhea in the third millennium: a pediatrician's perspective.**
  Author(s): Guandalini S.
  Source: Acta Gastroenterol Belg. 2002 January-March; 65(1): 33-6. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12014314&dopt=Abstract

- **Treatment of infectious diarrhea in children.**
  Author(s): Alam NH, Ashraf H.
  Source: Paediatric Drugs. 2003; 5(3): 151-65. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12608880&dopt=Abstract

- **Vitamin A supplementation and childhood morbidity from diarrhea and respiratory infections: a meta-analysis.**
  Author(s): Grotto I, Mimouni M, Gdalevich M, Mimouni D.
  Source: The Journal of Pediatrics. 2003 March; 142(3): 297-304.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12640379&dopt=Abstract

- **Women's management of the household health environment: responding to childhood diarrhea in the Northern Areas, Pakistan.**
  Author(s): Halvorson SJ.
  Source: Health & Place. 2004 March; 10(1): 43-58.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14637286&dopt=Abstract

- **Wood creosote, the principal active ingredient of seirogan, an herbal antidiarrheal medicine: a single-dose, dose-escalation safety and pharmacokinetic study.**
  Author(s): Kuge T, Shibata T, Willett MS.
  Source: Pharmacotherapy. 2003 November; 23(11): 1391-400.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14620385&dopt=Abstract

Additional Web Resources

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

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

The following is a specific Web list relating to diarrhea; 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**

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

  AIDS and HIV
  Source: Integrative Medicine Communications; www.drkoop.com

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

Allergic Rhinitis
Source: Integrative Medicine Communications; www.drkoop.com

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

Alzheimer's Disease
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

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

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

Bladder Infection
Alternative names: Urinary Tract Infection [UTI]
Source: Prima Communications, Inc.www.personalhealthzone.com

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

Bulimia Nervosa
Source: Integrative Medicine Communications; www.drkoop.com

Cancer Prevention (reducing the Risk)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

Chronic Obstructive Pulmonary Disease
Source: Integrative Medicine Communications; www.drkoop.com

Colds and Flus
Source: Prima Communications, Inc.www.personalhealthzone.com

Colorectal Cancer
Source: Integrative Medicine Communications; www.drkoop.com

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

Crohn's Disease
Source: Integrative Medicine Communications; www.drkoop.com

Diabetes Mellitus
Source: Integrative Medicine Communications; www.drkoop.com

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

Diverticular Disease
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

Epilepsy
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

Gallbladder Disease
Source: Integrative Medicine Communications; www.drkoop.com

Gastroesophageal Reflux Disease
Source: Integrative Medicine Communications; www.drkoop.com

Guinea Worm Disease
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Infantile Colic
Source: Integrative Medicine Communications; www.drkoop.com

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

Inflammatory Bowel Disease
Source: Integrative Medicine Communications; www.drkoop.com

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

Insect Bites and Stings
Source: Integrative Medicine Communications; www.drkoop.com

Intestinal Parasites
Source: Integrative Medicine Communications; www.drkoop.com

Iron-deficiency Anemia
Source: Healthnotes, Inc.; www.healthnotes.com

Irritable Bowel Syndrome
Source: Healthnotes, Inc.; www.healthnotes.com

Irritable Bowel Syndrome
Source: Integrative Medicine Communications; www.drkoop.com

Irritable Bowel Syndrome
Alternative names: Spastic Colon
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

Lymphatic Filariasis
Source: Integrative Medicine Communications; www.drkoop.com

Macular Degeneration
Source: Integrative Medicine Communications; www.drkoop.com

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

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

Menstrual Pain
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

Otitis Media
Source: Integrative Medicine Communications; www.drkoop.com

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

Peptic Ulcer
Source: Integrative Medicine Communications; www.drkoop.com

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

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

Prostate Cancer
Source: Integrative Medicine Communications; www.drkoop.com

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

Rectal Inflammation
Source: Integrative Medicine Communications; www.drkoop.com

River Blindness
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

Serum Sickness
Source: Integrative Medicine Communications; www.drkoop.com

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

Spastic Colon
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

Ulcerative Colitis
Source: Integrative Medicine Communications; www.drkoop.com

Urinary Tract Infection
Source: Healthnotes, Inc.; www.healthnotes.com

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

Visceral Larva Migrans
Source: Integrative Medicine Communications; www.drkoop.com

Vitamin B12 Deficiency
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

- **Alternative Therapy**

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

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

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

- **Chinese Medicine**

  Baibiandou
  Alternative names: White Hyacinth Bean; Semen Lablab Album
  Source: Chinese Materia Medica

  Baifan
  Alternative names: Alum; Baifan (Bai Fan); Alumen
  Source: Chinese Materia Medica

  Baizhu
  Alternative names: Largehead Atractylodes Rhizome; Rhizoma Atractylodis Macrocephalae
  Source: Chinese Materia Medica

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

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

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

  Binglang
  Alternative names: Areca Seed; Semen Arecae
  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

  Chansu
  Alternative names: Toad Venom; Venenum Bufonis
  Source: Chinese Materia Medica

  Chenpi
  Alternative names: Dried Tangerine Peel; Pericarpium Citri Reticulatae
  Source: Chinese Materia Medica

Cheqiancao
Alternative names: Plantain Herb; Herba Plantaginis
Source: Chinese Materia Medica

Cheqianzi
Alternative names: Plantain Seed; Semen Plantaginis
Source: Chinese Materia Medica

Chishizhi
Alternative names: Red Halloysite; Halloysitum Rubrum
Source: Chinese Materia Medica

Chuanmuxiang
Alternative names: Common Vladimiria root; Radix Vladimiriae
Source: Chinese Materia Medica

Chunpi
Alternative names: Tree-of-heaven Bark; Cortex Ailanthi
Source: Chinese Materia Medica

Daiwenjiu Gao
Alternative names: Daiwenjiu Plaster
Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

Dingxiang
Alternative names: Clove; Flos Caryophylli
Source: Chinese Materia Medica

Doukou
Alternative names: Round Cardamon Fruit; Fructus Amomi Rotundus
Source: Chinese Materia Medica

Fuling
Alternative names: Indian Bread; Poria
Source: Chinese Materia Medica

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

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

Ganjiang
Alternative names: Zingiber (Dried Ginger); Rhizoma Zingiberis
Source: Chinese Materia Medica

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

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

Gegen Qinlian Weiwan
Alternative names: Gegen Qinlian Micropilis
Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

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

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

Heye
Alternative names: Lotus Leaf; Folium Nelumbinis
Source: Chinese Materia Medica

Hezi
Alternative names: Medicine Terminalia Fruit; Fructus Chebulae
Source: Chinese Materia Medica

Hongdoukou
Alternative names: Galanga Galangal Fruit; Fructus Galangae
Source: Chinese Materia Medica

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

Hongqi
Alternative names: Manyinflorescenced Sweetvetch Root; Radix Hedysari
Source: Chinese Materia Medica

Houpo
Alternative names: Officinal Magnolia Bark; Cortex Magnoliae Officinalis
Source: Chinese Materia Medica

Huaijiao
Alternative names: Pricklyash Peel; Huajiao; Pericarpium Zanthoxyli
Source: Chinese Materia Medica

Huajiao
Alternative names: Pricklyash Peel; Pericarpium Zanthoxyli
Source: Chinese Materia Medica

Huangqi
Alternative names: Milkvetch; Radix Astragali
Source: Chinese Materia Medica

Huashi
Alternative names: Talc; Talcum
Source: Chinese Materia Medica

Hujiao
Alternative names: Pepper Fruit; Fructus Piperis
Source: Chinese Materia Medica

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

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

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

Jiguanhua
Alternative names: Cockcomb Flower; Flos Celosiae Cristatae
Source: Chinese Materia Medica

Jineijin
Alternative names: Chicken's Gizzard-skin; Endothelium Corneum Gigeriae Galli
Source: Chinese Materia Medica

Jinguolan
Alternative names: Tinospora Root; Radix Tinosporae
Source: Chinese Materia Medica

Jixuecao
Alternative names: Asiatic Pennywort Herb; Herba Centellae
Source: Chinese Materia Medica

Laifuzi
Alternative names: Radish Seed; Semen Raphani
Source: Chinese Materia Medica

Laoguancao
Alternative names: Common Heron's Bill Herb, Wilford Granesbill Herb; Herba ErodiiHerba Geranii
Source: Chinese Materia Medica

Lianzi
Alternative names: Szechwan Chinaberry Fruit; Chuanlianzi; Fructus Toosendan
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

Lujiaoshuang
Alternative names: Degelatined Deer-horn; Cornu Cervi Degelatinatum
Source: Chinese Materia Medica

Maohezi
Alternative names: Belleric Terminalia Fruit; Fructus Terminaliae Billericae
Source: Chinese Materia Medica

Mohanlian
Alternative names: Yerbadetajo Herb; Herba Ecliptae
Source: Chinese Materia Medica

Mugua
Alternative names: Common Floweringquince Fruit; Fructus Chaenomelis
Source: Chinese Materia Medica

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

Qiancao
Alternative names: Longtube Ground Ivy Herb; Lianqiancao; Herba Glechomae
Source: Chinese Materia Medica

Qianshi
Alternative names: Gordon Euryale Seed; Semen Euryales
Source: Chinese Materia Medica

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

Qinpi
Alternative names: Ash Bark; Cortex Fraxini
Source: Chinese Materia Medica

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

Quanshen
Alternative names: Bistort Rhizome; Rhizoma Bistortae
Source: Chinese Materia Medica

Renshen Jianpi Wan
Alternative names: Renshen Jianpi Pills; Renshen Jianpi Wan(Ren Shen Jian Pi Wan)
Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

Roudoukou
Alternative names: Nutmeg; Semen Myristicae
Source: Chinese Materia Medica

Rougui
Alternative names: Cassia Bark; Cortex Cinnamomi
Source: Chinese Materia Medica

Shanyao
Alternative names: Common Yam Rhizome; Rhizoma Dioscoreae
Source: Chinese Materia Medica

Shanzha
Alternative names: Hawthorn Fruit; Fructus Crataegi
Source: Chinese Materia Medica

Sharen
Alternative names: Villous Amomum Fruit; Fructus Amomi
Source: Chinese Materia Medica

Shayao
Alternative names: Shayao Pills; Shayao
(Sha Yao)
Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China
Hyperlink: http://www.newcenturynutrition.com/cgi-local/patent_herbs_db/db.cgi?db=default&Chinese=Shayao&mh=10&sb=---&view_records=View+Records

Shiliupi
Alternative names: Pomegranate Rind; Pericarpium Granati
Source: Chinese Materia Medica

Sini Tang
Alternative names: Sini Mixture; Sini Tang
(Si Ni Tang)
Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

Sishen Wan
Alternative names: Sishen Pills; Sishen Wan
(Si Shen Wan)
Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

Sizheng Wan
Alternative names: Sizheng Pills; Sizheng Wan
(Si Zheng Wan)
Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

Tumuxiang
Alternative names: Inula Root; Radix Inulae
Source: Chinese Materia Medica

Tusizi
Alternative names: Dodder Seed; Semen Cuseutae
Source: Chinese Materia Medica

Wubeizi
Alternative names: Chinese Gall; Galla Chinensis
Source: Chinese Materia Medica

Wumei
Alternative names: Smoked Plum; Fructus Mume
Source: Chinese Materia Medica

Wuweizi
Alternative names: Chinese Magnoliavine Fruit; Fructus Schisandrae
Source: Chinese Materia Medica

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

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

Xianmao
Alternative names: Common Curculigo Rhizome; Rhizoma Curculiginis
Source: Chinese Materia Medica

Xiaohuixiang
Alternative names: Fennel; Fructus Foeniculi
Source: Chinese Materia Medica

Yiyiren
Alternative names: Coix Seed; Semen Coicis
Source: Chinese Materia Medica

Yizhi
Alternative names: Sharpleaf Glangat Fruit; Fructus Alpiniae Oxyphyllae
Source: Chinese Materia Medica

Yuyuliang
Alternative names: Limonite; Limonitum
Source: Chinese Materia Medica

Zexie
Alternative names: Oriental Waterplantain Rhizome; Rhizoma Alismatis
Source: Chinese Materia Medica

Zhihongqi
Alternative names: Prepared Manyinflorescenced Sweetvetch Root; Radix Hedysari Preparata
Source: Chinese Materia Medica

Zhuling
Alternative names: Chuling; Polyporus
Source: Chinese Materia Medica

- **Homeopathy**

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

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

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

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

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

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

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

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

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

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

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

- **Herbs and Supplements**

5-hydroxytryptophan
Source: Healthnotes, Inc.; www.healthnotes.com

Acidophilus
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,748,00.html

Acidophilus and Other Probiotics
Source: Prima Communications, Inc.www.personalhealthzone.com

Activated Charcoal
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,832,00.html

Agrimony
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,833,00.html

Aloe
Alternative names: Aloe vera, Aloe barbadensis, Aloe ferox , Aloe Vera
Source: Integrative Medicine Communications; www.drkoop.com

Aloe Vera
Source: Integrative Medicine Communications; www.drkoop.com

Aloe Vera
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10001,00.html

Amino Acids
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10003,00.html

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

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

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

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

Ananas Comosus
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

Antibiotic Combination: Sulfa Drugs
Source: Integrative Medicine Communications; www.drkoop.com

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

Antibiotics (general)
Source: Prima Communications, Inc.www.personalhealthzone.com

Antituberculosis Agents
Source: Integrative Medicine Communications; www.drkoop.com

Aristolochia
Alternative names: Snakeroot, Guaco; Aristolochia sp
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

Arnica
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,753,00.html

Astragalus
Alternative names: Astragalus membranaceus
Source: Healthnotes, Inc.; www.healthnotes.com

Astragalus
Alternative names: Astragalus membranaceus, Astragalus membranaceus var. mongholicus, Huang-qi, Milk-Vetch Root
Source: Integrative Medicine Communications; www.drkoop.com

Astragalus Membranaceus
Source: Integrative Medicine Communications; www.drkoop.com

Astragalus Mongholicus
Alternative names: Astragalus membranaceus, Astragalus membranaceus var. mongholicus, Huang-qi, Milk-Vetch Root
Source: Integrative Medicine Communications; www.drkoop.com

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

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

Barberry
Alternative names: Berberis vulgaris
Source: Healthnotes, Inc.; www.healthnotes.com

Barberry
Alternative names: Berberis vulgaris, Berberry
Source: Integrative Medicine Communications; www.drkoop.com

Berberis
Alternative names: Barberry; Berberis sp.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

Berberis Vulgaris
Source: Integrative Medicine Communications; www.drkoop.com

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

Beta-carotene
Source: Prima Communications, Inc.www.personalhealthzone.com

Bilberry
Alternative names: Vaccinium myrtillus
Source: Healthnotes, Inc.; www.healthnotes.com

Bilberry
Alternative names: Vaccinium myrtillus, European Blueberry, Huckleberry
Source: Integrative Medicine Communications; www.drkoop.com

Bilberry
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10007,00.html

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

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

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

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

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

Black Snakeroot
Source: Integrative Medicine Communications; www.drkoop.com

Blackberry
Alternative names: Rubus fructicosus
Source: Healthnotes, Inc.; www.healthnotes.com

Blackberry
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,837,00.html

Bloodroot
Alternative names: Sanguinaria canadensis
Source: Healthnotes, Inc.; www.healthnotes.com

Blue Flag
Alternative names: Iris versicolor
Source: Healthnotes, Inc.; www.healthnotes.com

Blueberry
Alternative names: Vaccinium spp.
Source: Healthnotes, Inc.; www.healthnotes.com

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

Boswellia
Alternative names: Boswellia serrata
Source: Healthnotes, Inc.; www.healthnotes.com

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

Boswellia
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,759,00.html

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

Brewer's Yeast
Source: Healthnotes, Inc.; www.healthnotes.com

Bromelain
Alternative names: Ananas comosus, Bromelainum
Source: Integrative Medicine Communications; www.drkoop.com

Bromelain
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,760,00.html

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

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

Calcitrol
Source: Integrative Medicine Communications; www.drkoop.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

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

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

Cascara Sagrada
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10013,00.html

Cat's Claw
Alternative names: Uncaria tomentosa
Source: Integrative Medicine Communications; www.drkoop.com

Cayenne
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,765,00.html

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

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

Chamomile
Alternative names: Matricaria recutita
Source: Healthnotes, Inc.; www.healthnotes.com

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

Chinese Angelica
Source: Integrative Medicine Communications; www.drkoop.com

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

Cholecalciferol
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

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

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

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

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

Coenzyme Q
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,768,00.html

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

Cranberry
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10019,00.html

Cranesbill
Alternative names: Geranium maculatum
Source: Healthnotes, Inc.; www.healthnotes.com

Crataegus
Alternative names: Hawthorn; Crataegus oxyacantha L.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

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

Dandelion
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10021,00.html

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

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

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

Docetaxel
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

Dong Quai (angelica)
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,774,00.html

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

Echinacea
Alternative names: Echinacea purpurea, Echinacea angustifolia, Echinacea pallida
Source: Healthnotes, Inc.; www.healthnotes.com

Elderberry
Alternative names: Sambucus nigra
Source: Healthnotes, Inc.; www.healthnotes.com

Elderberry
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10024,00.html

Elecampane
Alternative names: Inula helenium
Source: Healthnotes, Inc.; www.healthnotes.com

Eleuthero
Alternative names: Eleutherococcus senticosus, Acanthopanax senticosus
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

European Blueberry
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

FOS
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10026,00.html

Fo-ti
Alternative names: Polygonum multiflorum
Source: Healthnotes, Inc.; www.healthnotes.com

Fructo-oligosaccharides (FOS) and Other Oligosaccharides
Source: Healthnotes, Inc.; www.healthnotes.com

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

Gentian
Alternative names: Gentiana lutea
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

Ginkgo Biloba
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,788,00.html

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

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

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

Glycyrrhiza1
Alternative names: Licorice; Glycyrrhiza glabra L.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

Goldenseal
Alternative names: Hydrastis canadensis
Source: Healthnotes, Inc.; www.healthnotes.com

Goldenseal
Alternative names: Hydrastis canadensis
Source: Integrative Medicine Communications; www.drkoop.com

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

Goldenseal
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,791,00.html

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

Grapefruit Seed Extract
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

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

Guggul
Alternative names: Commiphora mukul
Source: Healthnotes, Inc.; www.healthnotes.com

Gugulipid
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10033,00.html

He Shou Wu
Source: Prima Communications, Inc.www.personalhealthzone.com

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

Huang-qi
Source: Integrative Medicine Communications; www.drkoop.com

Huckleberry
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

Hydrastis Canadensis
Source: Integrative Medicine Communications; www.drkoop.com

Hypericum Perforatum
Alternative names: St. John's Wort
Source: Integrative Medicine Communications; www.drkoop.com

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

Indian Tobacco
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

Klamathweed
Alternative names: St. John's Wort
Source: Integrative Medicine Communications; www.drkoop.com

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

L. Acidophilus
Source: Integrative Medicine Communications; www.drkoop.com

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

Lactobacillus Acidophilus
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

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

Lobelia
Alternative names: Lobelia inflata, Indian Tobacco
Source: Integrative Medicine Communications; www.drkoop.com

Lobelia Inflata
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

Lysine
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,862,00.html

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

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

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

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

Matricaria
Alternative names: Chamomile; Matricaria chamomilla
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

Medium-chain Triglycerides
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

Milk Thistle
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10044,00.html

Milk-vetch Root
Source: Integrative Medicine Communications; www.drkoop.com

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

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

Motherwort
Alternative names: Leonurus cardiaca
Source: Healthnotes, Inc.; www.healthnotes.com

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

Mullein Flower
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,865,00.html

Musa Banana
Alternative names: Plantain, Banana; Musa sp.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

Nettle
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10048,00.html

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

Oak
Alternative names: Quercus spp.
Source: Healthnotes, Inc.; www.healthnotes.com

Oak Bark
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10108,00.html

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

Oregon Grape
Alternative names: Berberis aquifolium
Source: Healthnotes, Inc.; www.healthnotes.com

Paba
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10049,00.html

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

Passiflora Incarnata
Source: Integrative Medicine Communications; www.drkoop.com

Passionflower
Alternative names: Passiflora incarnata
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

Phytolacca
Alternative names: Poke root, Endod; Phytolacca dodecandra L.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

Plantago Isphagula
Source: Integrative Medicine Communications; www.drkoop.com

Plantago Psyllium
Alternative names: Psyllium, Ispaghula; Plantago psyllium/ovata
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

Potentilla
Alternative names: Cinquefoil, Silverweed; Potentilla sp.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

Psyllium
Alternative names: Plantago ovata, Plantago ispaghula
Source: Healthnotes, Inc.; www.healthnotes.com

Psyllium
Alternative names: Ispaghula,Plantago isphagula
Source: Integrative Medicine Communications; www.drkoop.com

Psyllium
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,814,00.html

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

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

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

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

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

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

Raspberry
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,1061,00.html

Red Raspberry
Alternative names: Rubus idaeus
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

Same (s-adenosylmethionine)
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,818,00.html

Sanguinaria
Alternative names: Bloodroot; Sanguinaria canadensis L.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

Senna
Alternative names: Cassia senna, Cassia angustifolia
Source: Healthnotes, Inc.; www.healthnotes.com

Shiitake
Alternative names: Lentinus edodes
Source: Healthnotes, Inc.; www.healthnotes.com

Siberian Ginseng
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,821,00.html

Slippery Elm
Alternative names: Ulmus rubra, Ulmus fulva
Source: Healthnotes, Inc.; www.healthnotes.com

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

Spirulina and Kelp
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10058,00.html

St. John's Wort
Alternative names: Hypericum perforatum
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

Sweet Annie
Alternative names: Artemisia annua
Source: Healthnotes, Inc.; www.healthnotes.com

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

Tetracycline Derivatives
Source: Integrative Medicine Communications; www.drkoop.com

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

Tilia Cordata
Source: Integrative Medicine Communications; www.drkoop.com

Tilia Platyphyllos
Source: Integrative Medicine Communications; www.drkoop.com

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

Trace Minerals
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10061,00.html

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

Trimethoprim/sulfamethoxazole
Source: Healthnotes, Inc.; www.healthnotes.com

Turmeric
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10062,00.html

Tylophora
Alternative names: Tylophora indica, Tylophora asthmatica
Source: Healthnotes, Inc.; www.healthnotes.com

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

Uncaria Tomentosa
Source: Integrative Medicine Communications; www.drkoop.com

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

Vaccinium Myrtillus
Source: Integrative Medicine Communications; www.drkoop.com

Wild Cherry
Alternative names: Prunus serotina
Source: Healthnotes, Inc.; www.healthnotes.com

Wild Yam
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10070,00.html

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

Yellow Dock
Alternative names: Rumex crispus
Source: Healthnotes, Inc.; www.healthnotes.com

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

Zanthoxylum
Alternative names: Prickly Ash; Zanthoxylum sp.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

Zingiber
Alternative names: Ginger; Zingiber officinale Roscoe
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

General References

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

CHAPTER 4. DISSERTATIONS ON DIARRHEA

Overview

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

Dissertations on Diarrhea

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 diarrhea. 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 Study of Diarrheal Illness and Its Correlates among Infants in Day Care in the Fifteen Southernmost Counties of Illinois** by Eichholz, Barbara, Phd from Southern Illinois University at Carbondale, 1986, 110 pages
  http://wwwlib.umi.com/dissertations/fullcit/8622974
- **A Study of the Mechanisms Responsible for Diarrhea in an Acute Viral Enteritis in Piglets, Transmissible Gastroenteritis** by Butler, Daniel George; Phd from University of Toronto (canada), 1974
  http://wwwlib.umi.com/dissertations/fullcit/NK26042
- **An Examination of the Effects of the Mother's Education and Household Exposure to Disease on Childhood Diarrheal Morbidity in Sudan** by Sultan, Dawood Hussein, Phd from The Louisiana State University and Agricultural and Mechanical Col., 1996, 160 pages
  http://wwwlib.umi.com/dissertations/fullcit/9706366

- **Association of Bovine Viral Diarrhea Virus with Day-7 Bovine Embryos Produced under Different Culture Conditions** by Jimenez Escobar, Claudia; Dvsc from University of Guelph (canada), 2002, 104 pages
  http://wwwlib.umi.com/dissertations/fullcit/NQ66111
- **Components of Infant and Childhood Mortality in West Africa: a Study of Health Care Practices, Breastfeeding Behavior and Its Interaction with Diarrhea, in Ghana and Nigeria** by Ahiadeke, Clement, Phd from Cornell University, 1996, 254 pages
  http://wwwlib.umi.com/dissertations/fullcit/9624870
- **Determinants of Childhood Diarrhea Morbidity and Mortality in Bobo-dioulasso, Burkina Faso** by Nacro, Kourtoum, Phd from The Florida State University, 1993, 186 pages
  http://wwwlib.umi.com/dissertations/fullcit/9402508
- **Development and Evaluation of Molecular Techniques for Diagnosis of Bovine Viral Diarrhea Virus** by Ahn, Byung Chul; Phd from Kansas State University, 2002, 166 pages
  http://wwwlib.umi.com/dissertations/fullcit/3076083
- **Diagnosis, Characterization, and Impact of Bovine Viral Diarrhea Virus (bvdv) Infection in Dairy Cattle under Field Management Conditions** by Munoz-zanzi, Claudia Andrea; Phd from University of California, Davis, 2002, 255 pages
  http://wwwlib.umi.com/dissertations/fullcit/3051546
- **Early Childhood Diarrhea and Primary School Performance in the Northern Areas of Pakistan** by Mitchell, Jonathan Eric, Phd from University of Colorado at Boulder, 1998, 254 pages
  http://wwwlib.umi.com/dissertations/fullcit/9916817
- **Environmental, Social-cultural, and Health Factors Associated with Diarrhea in Santa Cruz Mixtepec, Juxtlahuaca, Oaxaca, Mexico (growth, Contamination, Parasites, Vectors, Anthropometrics)** by Butler, Paula Merrell, Phd from The University of Tennessee, 1985, 165 pages
  http://wwwlib.umi.com/dissertations/fullcit/8600012
- **Feeding, Weaning, and Diarrhea Illness in Young Hausa Children in Niger: Village Practice and Educational Implications (young Children, Culturally Relevant Education)** by Keith, Nancy Jean, Phd from Michigan State University, 1991, 321 pages
  http://wwwlib.umi.com/dissertations/fullcit/9129467
- **Illness of the Child: the Cultural Context of Childhood Diarrhea in Northeast Brazil** by Nations, Marilyn Kay, Phd from University of California, Berkeley, 1982, 189 pages
  http://wwwlib.umi.com/dissertations/fullcit/8300729
- **Investigation of Bovine Viral Diarrhea Virus Pathogenesis** by Elsheikh, Abuelyazeed Abdelkader; Phd from South Dakota State University, 2002, 164 pages
  http://wwwlib.umi.com/dissertations/fullcit/3053944
- **Le Syndrome Diarrheique Chez Les Enfants Nahuas Du Mexique Une Approche Culturelle, Dietetique Et Medicale (french Text, Infants, Diarrhea, Mexico)** by Troche, Viviane, Phd from Universite De Montreal (canada), 1994, 563 pages
  http://wwwlib.umi.com/dissertations/fullcit/NN00344
- **Learning and Acting in a Health Communication Campaign: Teaching Rural Women to Prevent Infant Dehydration Through Diarrheal Disease Control in the Gambia, West Africa** by Snyder, Leslie Beth, Phd from Stanford University, 1986, 202 pages
  http://wwwlib.umi.com/dissertations/fullcit/8700821

- **Longitudinal Studies on the Epidemiology of Diarrheal Diseases in Peruvian Children** by Checkley, William N.; Phd from The Johns Hopkins University, 2002, 154 pages
  http://wwwlib.umi.com/dissertations/fullcit/3046431
- **Mechanism of Cold-induced Increase in Susceptibility to Enterotoxigenic Escherichia Coli-induced Diarrhea of the Newborn Pig** by Sarmiento, Juan Ignacio; Phd from University of Guelph (canada), 1986
  http://wwwlib.umi.com/dissertations/fullcit/NL28983
- **Parents' Responses to Children's Illnesses: the Case of Childhood Diarrhea in the Bakoum Area, Eastern Province, Cameroon** by Mbeh, George Ngong; Phd from University of Florida, 1999, 205 pages
  http://wwwlib.umi.com/dissertations/fullcit/9976576
- **Risk Factors for Diarrheal Disease in Village Children in Nepal (child Survival)** by Laston, Sandra Lee, Phd from Case Western Reserve University, 1992, 428 pages
  http://wwwlib.umi.com/dissertations/fullcit/9220048
- **Social Influence As a Component of Contextual Effects: a Study of Diarrheal Treatment in Zaire** by Zheng, Zhong, Phd from University of Pennsylvania, 1994, 218 pages
  http://wwwlib.umi.com/dissertations/fullcit/9427641
- **Spatial and Environmental Risk Factors for Diarrheal Disease in Matlab, Bangladesh** by Emch, Michael Edward, Phd from Michigan State University, 1998, 184 pages
  http://wwwlib.umi.com/dissertations/fullcit/9839637
- **The Application of Social Marketing in the Prevention of Diarrheal Diseases: the Case of Mexico** by Cervantes-aldana, Fernando Javier, Phd from The University of Texas at Austin, 1980, 344 pages
  http://wwwlib.umi.com/dissertations/fullcit/8109142
- **The Decline in Diarrhea-related Infant Mortality in San Antonio, Texas, 1935 to 1954: the Role of Sanitation** by Blanchard, Kenneth Stephen, Jr., Phd from The University of Texas at Austin, 1996, 258 pages
  http://wwwlib.umi.com/dissertations/fullcit/9705797
- **The Epidemiology of Acute Undifferentiated Diarrhea of Beef Calves in Western Canada** by Acres, Stephen Douglas; Phd from The University of Saskatchewan (canada), 1977
  http://wwwlib.umi.com/dissertations/fullcit/NK31675
- **The Household Management of Childhood Diarrhea in Rural North India** by Bentley, Margaret Esplin, Phd from The University of Connecticut, 1987, 414 pages
  http://wwwlib.umi.com/dissertations/fullcit/8811726
- **The Overuse of Drugs in the Treatment of Childhood Diarrhea: Its Determinants and a Potential Intervention** by Paredes-solari, Patricia; Drph from The Johns Hopkins University, School of Public Health and Hygiene, 2002
  http://wwwlib.umi.com/dissertations/fullcit/f754737
- **The Politics Ofumoya: Variation in the Interpretation and Management of Diarrheal Illnesses among Mothers, Professional Nurses, and Indigenous Health Practitioners in Khayelitsha, South Africa** by Guma, Mthobeli Phillip, Phd from The University of North Carolina at Chapel Hill, 1998, 272 pages
  http://wwwlib.umi.com/dissertations/fullcit/9840918

- **The Rotavirus of Neonatal Calf Diarrhea : Some Parameters of Pathogenesis and Diagnosis** by Mohammed, Khalid A; Phd from The University of Saskatchewan (canada), 1977
  http://wwwlib.umi.com/dissertations/fullcit/NK36933
- **The Treatment of Childhood Diarrhea in Managua, Nicaragua (diarrhea)** by Hudelson, Patricia Martha, Phd from The University of Connecticut, 1989, 237 pages
  http://wwwlib.umi.com/dissertations/fullcit/9008787

Keeping Current

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

CHAPTER 5. CLINICAL TRIALS AND DIARRHEA

Overview

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

Recent Trials on Diarrhea

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

- **A Randomized Trial of Tap Water Treatment in the Elderly**

  Condition(s): Diarrhea; Gastrointestinal Diseases

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute on Aging (NIA)

  Purpose - Excerpt: This study is being conducted in Sonoma County, California. Gastrointestinal illness and **diarrhea** are recognized as a significant cause of morbidity and mortality in the elderly. One study showed that 51% of deaths caused by **diarrhea** over a 9-year period occurred in individuals over the age of 74 years. Although many infectious diseases are more problematic in the elderly because of a decline in immune function and a higher incidence of pre-existing malnutrition and dehydration, it is still not known what the principal modes of transmission are and which infectious agents are responsible. The principal objective of this study is to evaluate the ability of in-home treatment of tapwater to reduce gastrointestinal illness in non-institutionalized elderly individuals. The trial will test household-level treatment of drinking water by joint use of ultraviolet light and filtration devices. A secondary objective is an estimate of the incidence of specific bacterial, viral, and protozoan agents in stool specimens collected from elderly individuals with gastrointestinal symptoms that might be related to water consumption.

  Study Type: Interventional

  Contact(s): see Web site below

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

Web Site: http://clinicaltrials.gov/ct/show/NCT00058942

- **A Study to Evaluate the Use of Nitazoxanide to Treat Cryptosporidiosis (Diarrhea Caused by the Parasite Cryptosporidium)**

  Condition(s): Cryptosporidiosis; HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Romark Laboratories L.C.

  Purpose - Excerpt: The purpose of this study is to see if nitazoxanide (NTZ) can be used to treat AIDS patients suffering from cryptosporidiosis (diarrhea caused by the parasite Cryptosporidium).

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002158

- **Acupuncture and Moxa: A RCT for Chronic Diarrhea in HIV Patients**

  Condition(s): HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Center for Complementary and Alternative Medicine (NCCAM); National Institute of Nursing Research (NINR)

  Purpose - Excerpt: The objective of this study is to test alternative treatment strategies to reduce the frequency of chronic diarrhea among HIV positive individuals. 60 percent of patients with HIV disease in the U.S. will have diarrhea at some point in their illness. Although in general many of the opportunistic infections (OI's) associated with HIV have decreased due to new "drug cocktails", many of these drugs, however, have diarrhea as a side effect. In Asian countries, acupuncture (including moxibustion) has been widely used for the treatment of various gastrointestinal (GI) disorders. However, there are no published studies that test treatment protocols using acupuncture or moxibustion on patients with HIV experiencing chronic diarrhea.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00010491

- **Genetic Trial to Study Diarrhea in Patients With Stage III Colon Cancer Who Are Receiving Chemotherapy**

  Condition(s): adenocarcinoma of the colon; stage III colon cancer; Diarrhea; Neutropenia

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Cancer and Leukemia Group B; National Cancer Institute (NCI); North Central Cancer Treatment Group

  Purpose - Excerpt: RATIONALE: Genetic testing may help predict how patients will respond to chemotherapy drugs and may help doctors plan more effective treatment with fewer side effects. PURPOSE: Genetic study to determine how genes affect the severity of diarrhea in patients with stage III colon cancer who are receiving chemotherapy.

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00048971

- **Octreotide in Preventing Diarrhea in Patients Who Are Undergoing Radiation Therapy to the Pelvis**

  Condition(s): adult solid tumor; Diarrhea; Endocrine Cancer; female reproductive cancer; Gastrointestinal Cancer; male reproductive cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): North Central Cancer Treatment Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Octreotide may be effective in preventing or controlling diarrhea in patients who are undergoing radiation therapy to the pelvis. It is not yet known whether octreotide is effective for diarrhea. PURPOSE: Randomized phase III trial to determine the effectiveness of octreotide in preventing diarrhea in patients who are undergoing radiation therapy to the pelvis.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00033605

- **Safety Study of the Chemotherapy Modulator PHY906 in Patients With Advanced Colorectal Cancer**

  Condition(s): Colorectal Neoplasms; Diarrhea

  Study Status: This study is currently recruiting patients.

  Sponsor(s): PhytoCeutica

  Purpose - Excerpt: The triple combination chemotherapy of irinotecan, 5-fluorouracil and leucovorin (CPT-11/5-FU/LV or Saltz regimen) is the treatment of choice for patients with advanced colorectal cancer. Severe **diarrhea,** unfortunately, is a side effect of such treatment. Preclinical studies have indicated that the botanical drug PHY906 can reduce such **diarrhea** without compromising the effectiveness of the chemotherapy. The primary purpose of this clinical study is to evaluate the safety, tolerability and minimum effective dose of PHY906 when administered in conjunction with the Saltz regimen.

  Phase(s): Phase I; Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00036517

- **STOP Trial - Sandostatin LAR Depot Trial for the Optimum Prevention of Chemotherapy Induced Diarrhea**

  Condition(s): Neoplasms; Diarrhea

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Novartis Pharmaceuticals; Quintiles

Purpose - Excerpt: Currently there is an ongoing clinical trial for patients with chemotherapy induced diarrhea. This trial is being conducted to evaluate the efficacy of two dose levels (30 mg and 40 mg) of an investigational drug in reducing the occurrence of severe (Grade 3 or 4) diarrhea during chemotherapy. Eligible patients must either have experienced NCI Common Toxicity Grade 1 - 4 chemotherapy-induced diarrhea during previous chemotherapy treatment or be experiencing Grade 1-4 chemotherapy-induced diarrhea currently. In order to participate in this clinical trial, patients must be male or female 18 years of age or older. Inclusion into this investigational drug trial is based on the protocol entry criteria and a detailed evaluation from a participating trial investigator

Phase(s): Phase IV

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00050635

- **Study In Women With Severe Diarrhea-Predominant Irritable Bowel Syndrome Having Failed Conventional Therapy**

  Condition(s): Irritable Bowel Syndrome

  Study Status: This study is currently recruiting patients.

  Sponsor(s): (Sponsor Name Pending)

  Purpose - Excerpt: The purpose of this study is to compare the safety and effectiveness of as needed versus fixed dosing of an investigational medication for women with severe diarrhea-predominant Irritable Bowel Syndrome (IBS) who have failed conventional therapy.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00067457

- **Study Of Women With Severe Diarrhea-Predominant Irritable Bowel Syndrome Having Failed Conventional Therapy**

  Condition(s): Irritable Bowel Syndrome

  Study Status: This study is currently recruiting patients.

  Sponsor(s): (Sponsor Name Pending)

  Purpose - Excerpt: The purpose of this study is to compare the safety and effectiveness of different doses of an investigational medication in women with severe diarrhea-predominant Irritable Bowel Syndrome (IBS) who have failed conventional therapy.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00067561

- **The Healthy Life Choices Project in HIV-Positive Patients**

  Condition(s): Diarrhea; HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Nursing Research (NINR)

  Purpose - Excerpt: The purpose of this study is to see whether changes in diet and behavior lessen the number of times HIV-positive people get **diarrhea** (soft or loose stools).

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00017810

- **Nitazoxanide for the Treatment of Chronic Diarrhea in HIV Infected Children**

  Condition(s): HIV Infections; Cryptosporidiosis

  Study Status: This study is not yet open for patient recruitment.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID); National Institute of Child Health and Human Development (NICHD)

  Purpose - Excerpt: Cryptosporidium parvum (C. parvum) is a parasite that can cause chronic diarrhea and is a significant problem for HIV infected children in developing countries. C. parvum infection can be treated with the drug nitazoxanide (NTZ). However, NTZ has not been tested in HIV infected children. This study will test the safety of giving NTZ to HIV infected children who have chronic diarrhea caused by C. parvum.

  Phase(s): Phase I; Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00055107

- **Octreotide in Preventing Diarrhea in Patients Receiving Chemotherapy for Colorectal Cancer**

  Condition(s): Colon Cancer; Diarrhea; Rectal Cancer

  Study Status: This study is not yet open for patient recruitment.

  Sponsor(s): University of Rochester; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Octreotide may be effective in preventing or controlling diarrhea in patients who are receiving chemotherapy for colorectal cancer. It is not yet known whether octreotide is more effective than standard treatment for diarrhea. PURPOSE: Randomized phase III trial to compare the effectiveness of octreotide with that of standard therapy in preventing diarrhea in patients who are receiving chemotherapy for colorectal cancer.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00052975

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 "diarrhea" (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 DIARRHEA

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.[9] Patents, therefore, are intellectual property. For the United States, the term of a new patent is 20 years from the date when the patent application was filed. If the inventor wishes to receive economic benefits, it is likely that the invention will become commercially available within 20 years of the initial filing. It is important to understand, therefore, that an inventor's patent does not indicate that a product or service is or will be commercially available. The patent implies only that the inventor has "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States. While this relates to U.S. patents, similar rules govern foreign patents.

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

Patents on Diarrhea

By performing a patent search focusing on diarrhea, 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

[9] 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 diarrhea:

- **1,4-dithiin and 1,4-dithiepin-1,1,4,4, tetroxide derivatives useful as antagonists of the human galanin receptor**

  Inventor(s): Lee; Daniel H. S. (Northampton, PA), Reitz; Allen B. (Lansdale, PA), Ross; Tina Morgan (Audubon, PA), Scott; Malcolm K. (Lansdale, PA), Wang; Haou-Yan (Philadelphia, PA)

  Assignee(s): Ortho-McNeil Pharmaceutical, Inc. (Raritan, NJ)

  Patent Number: 6,407,136

  Date filed: May 2, 2000

  Abstract: The invention is directed to 1,4-dithiin- and 1,4-dithiepin-1,1,4,4-tetroxide derivatives useful as galanin receptor antagonists for treating disorders of the central nervous system. Pharmaceutical compositions comprising the compounds of the present invention and methods of treating conditions such as an eating disorder, obesity, bulimia nervosa, anorexia nervosa, binge eating, diabetes, dyslipidemia, hypertension, memory loss, sleep disturbances, pain, depression, anxiety, Alzheimer's disease, senile dementia, cerebral hemorrhage, or **diarrhea** are also described.

  Excerpt(s): This invention relates to a series of 1,4-dithiin- and 1,4-dithiepin-1,1,4,4-tetroxide derivatives and their use for the treatment of central nervous system disorders and affective conditions. More particularly, the compounds of the invention are ligands for the human galanin receptor. The galanin neuropeptide is a 29-30 amino acid peptide that is found in mammalian central (CNS) and peripheral (PVS) nervous systems (Bartfai, T.; Hokfelt, T.; Langel, U., Galanin-A Neuroendocrine Peptide. Crit. Rev. Neurobiol., 1993, 7, 229-274; Crawley, J. N., Biological Actions of Galanin, Regulatory Neuropeptides, 1995, 59, 1-16; Kask, K.; Berthold, M.; Bartfai, T., Galanin Receptors: Involvement in Feeding, Pain, Depression, and Alzheimer's Disease. Life Sci., 1997, 60,1523-1533). In the CNS, galanin is distributed in axons and neurons located in the thalamus, hypothalamus, cortex, amygdala, hippocampus and spinal cord (Melander, T.; Hokfelt, T.; Rokaeus, A., Distribution of Galanin-like Immunoreactivity in the Rat Central Nervous System. J. Comp. Neurol, 1986, 248, 475-517; Skofitsch, G.; Jacobowitz, D. M., Immunohistochemical Mapping of Galanin-like Neurons in the Rat Central Nervous System. Peptides, 1985, 6, 509-516), while in the PVS, it is found in pancreas, gastrointestinal, bladder, and genital tissue (Rokaeus, A., Galanin: A Newly Isolated Biologically Active Peptide. Trends Neurosci., 1987, 10, 158-164). The effects of galanin in mammalian CNS are due to its interaction with at least three galanin receptors, GalR1, GalR2, and GalR3 which have been isolated, characterized, and cloned (Wang, S., Parker, E. M., Galanin Receptor Subtypes as Potential Therapeutic Targets. Exp. Opin. Ther. Patents, 1998, 8, 1225-1335 and references therein). While GalR1 is predominately found in the CNS, GalR2 and GalR3 are also present in small amounts.

  Web site: http://www.delphion.com/details?pn=US06407136__

- **4-[aryl(8-azabicyclo[3.2.1]octan-3-yl)]aminobenzoic acid derivatives**

  Inventor(s): Boyd; Robert E. (Horsham, PA), Carson; John R. (Norristown, PA), Neilson; Lou Anne (Sellersville, PA)

  Assignee(s): Ortho-McNeil Pharmaceutical, Inc. (Raritan, NJ)

  Patent Number: 6,306,876

  Date filed: December 4, 2000

  Abstract: 4-[aryl(8-azabicyclo[3.2.1]octan-3yl)]aminobenzoic acid derivatives are delta-opioid receptor modulators. As delta-opioid receptor agonists, such compounds are useful as analgesics. Depending on their antagonist effect, such compounds may also be useful immunosuppressants, antiinflammatory agents, agents for the treatment of neurological and psychiatric conditions, medicaments for drug and alcohol abuse, agents for treating gastritis and **diarrhea,** cardiovascular agents and agents for the treatment of respiratory diseases.

  Excerpt(s): The present invention is directed to delta-opioid receptor modulators. More particularly, the present invention is directed to 4-[aryl(8-azabicyclo[3.2.1]octan-3-yl)]aminobenzoic acid derivatives which are delta-opioid receptor modulators useful as effective analgesics. The foregoing reference compounds have been described as either delta- or mu-opioid receptor agonists or antagonists. It is an object of the present invention to provide delta-opioid receptor modulators. It is another object of the present invention to provide delta-opioid receptor selective agonists as analgesics having reduced side-effects. It is also another object of the present invention to provide delta-opioid receptor antagonists as immunosuppressants, antiinflammatory agents, agents for the treatment of neurological and psychiatric conditions, medicaments for drug and alcohol abuse, agents for treating gastritis and **diarrhea,** cardiovascular agents and agents for the treatment of respiratory diseases, having reduced side-effects. It is a further object of the present invention to provide a method for treating a disorder modulated by the delta-opioid receptor.

  Web site: http://www.delphion.com/details?pn=US06306876__

- **4-[aryl(piperidin-4-yl)]aminobenzamides**

  Inventor(s): Carmosin; Richard J. (late of Quakertown, PA), Carson; John R. (Norristown, PA), Fitzpatrick; Louis J. (Souderton, PA), Jetter; Michele C. (Norristown, PA), Reitz; Allen B. (Lansdale, PA)

  Assignee(s): Ortho-McNeil Pharmaceutical, Inc. (Raritan, NJ)

  Patent Number: 6,436,959

  Date filed: December 23, 1998

  Abstract: 4-[aryl(piperidin-4-yl)]aminobenzamides are delta-opioid receptor agonists/antagonists. As delta-opioid receptor agonists, such compounds are useful as analgesics. Depending on their agonist/antagonist effect, such compounds may also be useful immunosuppressants, antiinflammatory agents, agents for the treatment of mental illness, medicaments for drug and alcohol abuse, agents for treating gastritis and **diarrhea,** cardiovascular agents, and agents for the treatment of respiratory diseases.

  Excerpt(s): The present invention relates to delta-opioid receptor agonists/antagonists. More particularly, the present invention relates to 4-[aryl(piperidin-4-

yl)]aminobenzamides which are delta-opioid receptor agonists useful as analgesics. which are mu-opioid antagonists. which are delta-opioid agonists/antagonists.

Web site: http://www.delphion.com/details?pn=US06436959__

- **Alleles of the human mu opioid receptor and diagnostic methods based thereon**

  Inventor(s): Kreek; Mary Jeanne (New York, NY), LaForge; Karl Steven (New York, NY), Tischfield; Jay A. (Carmel, IN), Yu; Lei (Cincinnati, OH)

  Assignee(s): The Advanced Research and Technology Institute, Inc. (Bloomington, IN), The Rockefeller University (New York, NY)

  Patent Number: 6,335,168

  Date filed: July 9, 1999

  Abstract: Provided herein are variant alleles of a gene encoding a mu opioid receptor, along with cloning vectors for replicating such variant alleles, expressing vectors for expressing the variant alleles to produce variant mu opioid receptors, and antibodies to such variant receptors. Also disclosed are binding characteristics of such variant receptors regarding binding to opioid ligands, and the using of such binding characteristics to diagnose a subjects susceptibility to pain, susceptibility to an addictive disease, selecting an appropriate pain reliever along with a therapeutically effective amount of the reliever to administer to a subject suffering from pain. In addition, diagnostic methods for diagnosing a disease or disorder such as infertility, constipation, **diarrhea,** decreased immune response relative to a standard, and decreased ability to withstand stress relative to a standard, along with commercial kits for diagnosing such diseases or disorders. Furthermore, the invention is also directed to identification of targeted prevention methods, early therapeutic intervention, and improved treatment of opioid addiction, infertility, constipation, **diarrhea,** impaired immune responsiveness, and stress.

  Excerpt(s): This invention relates generally to alleles of the human mu opioid receptor gene, along with products derived from such alleles. Also included herein are methods of diagnosing various susceptibilities using such alleles and determining treatment for certain diseases based upon the presence of specific alleles of the human mu opioid receptor gene, and various diseases or disorders related to physiological functions regulated by the hypothalamus pituitary adrenal axis (HPA) or the hypothalamus pituitary gonadal axis (HPG). Opioid drugs have various effects on perception of pain, consciousness, motor control, mood, autonomic function, and can also induce physical dependence. The endogenous opioid system plays an important role in modulating endocrine, cardiovascular, respiratory, gastrointestinal functions, and immune functions. Opioids, either exogenous or endogenous, exert their actions by binding to specific membrane-associated receptors. Examples of exogenous opioids presently known include, opium, heroin, morphine, codeine, fentanyl, and methadone, to name only a few. Moreover, a family of over 20 endogenous opioid peptides has been identified, wherein the members possess common structural features, including a positive charge juxtaposed with an aromatic ring that is required for interaction with an opioid receptor. It has been determined that most, if not all the endogenous opioid peptides are derived from the proteolytic processing of three precursor proteins, i.e., prbopiomelanocortin, proenkephalin, and prodynorphin. In addition, a fourth class of endogenous opioids, the endorphins, has been identified (the gene encoding these proteins has not yet been cloned). In the processing of the endogenous opioid precursor proteins, initial cleavages are made by membrane-bound proteases that cut next to pairs

of positively charged amino acid residues, and then trimming reactions produce the final endogenous opioids secreted from cells in vivo. Different cell types contain different processing enzymes so that, for example proopiomelanocortin can be processed into different endogenous peptides by different cells. For example, in the anterior lobe of the pituitary gland, only corticotropin (ACTH),.beta.-lipotropin, and.beta.-endorphin are produced. Both pro-enkephalin and pro-dynorphin are similarly processed by specific enzymes in specific cells to yield multiple opioid peptides.

Web site: http://www.delphion.com/details?pn=US06335168__

- **Berberine alkaloids as a treatment for chronic protozoally induced diarrhea**

  Inventor(s): McDevitt; Joseph T. (Villanova, PA)

  Assignee(s): PRM Pharmaceuticals, Inc. (Ardmore, PA)

  Patent Number: 6,280,768

  Date filed: July 1, 1997

  Abstract: A method for the treatment or prevention of chronic **diarrhea** caused by protozoa, especially microsporidia and cryptosporidia, in a patient is disclosed which method comprises administering to the patient an effective amount of a berberine alkaloid. The administration of the berberine alkaloid may be in combination with one or more antiprotozoal agents other than berberine.

  Excerpt(s): Diarrhea is generally described according to several criteria: duration (acute vs. chronic), clinical description (frequency, water content, presence of blood), and etiology. Chronic **diarrhea** has been described as two to three or more loose or **watery stools** per day for a period of at least 30 days. It is important to distinguish chronic **diarrhea** from acute **diarrhea.** Chronic **diarrhea** is a distinct clinical entity from acute **diarrhea** that, if unchecked, results in morphological and functional pathology in the intestine. As opposed to acute **diarrhea,** histological examination of the chronically infected small intestinal mucosa reveals villus atrophy, crypt hypertrophy, and decreased mitosis. Chronic **diarrhea** leads to malabsorption, weight loss and cachexia. Both the World Health Organization (WHO) and the Center for Disease Control (CDC) have recognized this condition as the "Diarrhea Wasting Syndrome". It is often possible to trace the cause of the clinical symptoms of chronic **diarrhea** in immunosuppressed patients to one or more organisms found in the intestinal tract. In these immunosuppressed individuals, microbes which are relatively harmless to the normal individual take advantage of the very weak immune response to establish a persistent opportunistic infective state. For example, in immunosuppressed patients, such as those with Acquired Immunodeficiency Syndrome (AIDS), chronic **diarrhea** has been ascribed to the presence of the HIV virus itself, to cytomegalovirus, to the presence of various toxic bacteria, and frequently to infection by pathogenic protozoa. Prevalent among the pathogenic protozoa associated with the presence of **diarrhea** in immunosuppressed patients are intracellular microsporidia and cryptosporidia (Goodgame, R. W. Ann. Int. Med. 124:429-441 (1996)). In healthy individuals, microsporidial and cryptosporidial infections are self-limiting but immunosuppressed patients can not mount an effective enough immune response to eliminate the causative organism.

  Web site: http://www.delphion.com/details?pn=US06280768__

- **Contulakin-G, analogs thereof and uses therefor**

  Inventor(s): Craig; A. Grey (Solana Beach, CA), Cruz; Lourdes J. (Salt Lake City, UT), Griffin; David (Greenville, NC), Hillyard; David R. (Salt Lake City, UT), Imperial; Julita (Salt Lake City, UT), Jones; Robert M. (Salt Lake City, UT), Layer; Richard T. (Sandy, UT), McCabe; R. Tyler (Salt Lake City, UT), Olivera; Baldomero M. (Salt Lake City, UT), Wagstaff; John D. (Salt Lake City, UT), Watkins; Maren (Salt Lake City, UT)

  Assignee(s): University of Utah Research Foundation (Salt Lake City, UT)

  Patent Number: 6,344,551

  Date filed: June 29, 2000

  Abstract: The present invention is directed to contulakin-G (which is the native glycosylated peptide), a des-glycosylated contulakin-G (termed Thr.sub.10 -contulakin-G), and derivatives thereof, to a cDNA clone encoding a precursor of this mature peptide and to a precursor peptide. The invention is further directed to the use of this peptide as a therapeutic for anti-seizure, anti-inflammatory, anti-shock, anti-thrombus, hypotensive, analgesia, anti-psychotic, Parkinson's disease, gastrointestinal disorders, depressive states, cognitive dysfunction, anxiety, tardive dyskinesia, drug dependency, panic attack, mania, irritable bowel syndrome, **diarrhea,** ulcer, GI tumors, Tourette's syndrome, Huntington's chorea, vascular leakage, anti-arteriosclerosis, vascular and vasodilation disorders, as well as neurological, neuropharmalogical and neuropsychopharmacological disorders.

  Excerpt(s): The publications and other materials used herein to illuminate the background of the invention, and in particular, cases to provide additional details respecting the practice, are incorporated by reference, and for convenience are numerically referenced in the following text and respectively grouped in the appended bibliography. Mollusks of the genus Conus produce a venom that enables them to carry out their unique predatory lifestyle. Prey are immobilized by the venom that is injected by means of a highly specialized venom apparatus, a disposable hollow tooth that functions both in the manner of a harpoon and a hypodermic needle.

  Web site: http://www.delphion.com/details?pn=US06344551__

- **Diarrhea mitten**

  Inventor(s): Schaetzel; Mary Alice (1022 Silver Spruce, Arlington, TX 76017)

  Assignee(s): none reported

  Patent Number: 6,516,469

  Date filed: October 13, 2000

  Abstract: The present invention discloses a sanitary handwear being a hygienic mitten to be worn about the hand of the user for protection of the hand of the user to be used to clean, wipe babies, self, or older people with bowel control problems. The present invention has a single compartment to house all of the fingers of the hand and a separate compartment for the thumb and has a defined wrist area. The mitten of the present invention is made of two layers. The first, inner layer is waterproof and impermeable, and, the second, outer layer is a moist, extra absorbent cloth-like disposable material containing moisturizers. The mitten is comprised of disposable material so that it may be easily and economically disposed of after use. The mitten also has an internal pull tab to aid in removal of the glove from the hand of the user.

Excerpt(s): The present invention relates generally to the field of hand protection, more particularly, to protective hygienic mittens to be worn by a user to protect his hands from human waste material as the user performs hygienic care of the body of a baby, older person or self. Protective handwear has been described in the prior art. However, none of the prior art devices disclose the unique features of the present invention. In U.S. Pat. No. 5,732,413, dated Mar. 31, 1998, Williams disclosed an article of clothing and the method of making the same which will allow water vapor due to perspiration to transpire through the article but will prevent liquid water from external sources from reaching the wearer's extremity. One form of the article of the invention comprises a sock which is of three-ply construction with the inside and outside plies being knit and the intermediate ply being made from a stretch and return polyurethane film. The three plies are uniquely bonded together using a pliant, waterproof adhesive. Another form of the mandrel comprises a glove which is of a similar three-ply construction.

Web site: http://www.delphion.com/details?pn=US06516469__

- **Diarylsulfonylureas for use in treating secretory diarrhea**

  Inventor(s): Schultz; Bruce D (Wamego, KS)

  Assignee(s): Eli Lilly and Company (Indianapolis, IN)

  Patent Number: 6,281,240

  Date filed: January 31, 2000

  Abstract: This invention provides methods of treating secretory **diarrhea** or cystic fibrosis in a mammal which comprises administering to a mammal in need thereof an effective amount of diarylsulfonylurea. This invention also describes specific diarylsulfonylureas for use in treating secretory **diarrhea** or cystic fibrosis.

  Excerpt(s): The present understanding of the underlying pathophysiological mechanism of acute secretory **diarrhea** is growing steadily. Secretory **diarrhea** can accompany gastrointestinal disorders such as inflammatory bowel disease. Acute **diarrhea** is a world-wide problem, and easily accounts for over a million deaths per year. Medical and pharmacological textbooks generally delineate two classifications for anti-diarrheal medications. The first group are known as astringents. The second group are opium derivatives. While such medications have met with some degree of success, it is an alarming fact that drug development specifically targeting diarrheal disease has been, until recently, almost nonexistent. Probably the most significant event in the treatment of diarrheal disease in the past one hundred years has been the use of oral glucose-electrolyte solutions. But, there still is a need recognized by world-wide health organizations for continuing effort in **diarrhea** therapies. Recent studies of electrolyte transport by intestinal mucosa have provided valuable information concerning the regulation of biochemical events involved in **diarrhea.** While there is still much refinement work needed, it has now become apparent that a method of treatment of **diarrhea** would be to control electrolyte transport, particularly chloride secretion.

  Web site: http://www.delphion.com/details?pn=US06281240__

- **Hepatitis C virus protease-dependent chimeric pestivirus**

  Inventor(s): Hong; Zhi (Nanuet, NY), Lai; Vicki C. H. (North Plainfield, NJ), Lau; Johnson Y. N. (Warren, NJ)

  Assignee(s): Schering Corporation (Kenilworth, NJ)

  Patent Number: 6,326,137

  Date filed: June 25, 1999

  Abstract: A chimeric bovine viral **diarrhea** virus (BVDV) that depends on a hepatitis C virus (HCV). The invention further relates to using the chimeric, infectious virus to screen for HCV NS3 inhibitor compounds in cell culture models or in animal models of viral infection.

  Excerpt(s): The present invention relates to a chimeric pestivirus, such as bovine viral **diarrhea** virus (BVDV), that depends on a hepatitis C virus (HCV) protease function. The invention further relates to using the chimeric, infectious virus to screen for HCV NS3 inhibitor compounds in cell culture systems or in animal models of viral infection. Infection by hepatitis C virus (HCV) is a compelling human medical problem. HCV is recognized as the causative agent for most cases of non-A and non-B hepatitis, with an estimated prevalence of 170 million cases (i.e., 2-3%) globally [Choo, et al., Science, 244: 359-362 (1989); Kuo, et al., Science, 244: 362-364 (1989); Purcell, FEMS Microbiology Reviews, 14: 181-192 (1994); Van der Poel, C. L., Current Studies in Hematology and Blood Transfusion, H. W. Reesink, Ed., (Basel: Karger), pp. 137-163 (1994)]. Four million individuals may be infected in the United States alone [Alter, and Mast, Gastroenterol. Clin. North Am., 23: 437-455 (1994)]. Upon first exposure to HCV only about 10% or less of infected individuals develop acute clinical hepatitis, while others appear to resolve the infection spontaneously. In the most instances, however, the virus establishes a chronic infection that persists for decades [Iwarson, FEMS Microbiology Reviews, 14: 201-204 (1994)]. This usually results in recurrent and progressively worsening liver inflammation, which often leads to more severe disease states such as cirrhosis and hepatocellular carcinoma [Kew, FEM Microbiology Reviews, 14: 211-220 (1994); Saito, et al., Proc. Natl. Acad. Sci. USA 87:6547-6549 (1990)]. Currently, there are no broadly effective treatments for the debilitating progression of chronic HCV.

  Web site: http://www.delphion.com/details?pn=US06326137__

- **Lactobacillus bifidus growth promoting composition and use thereof**

  Inventor(s): Hayasawa; Hirotoshi (Kanagawa, JP), Nakamura; Hirohiko (Kanagawa, JP), Ohashi; Toshio (Kanagawa, JP), Sayama; Koji (Hokkaido, JP), Takase; Mitsunori (Kanagawa, JP), Tomita; Mamoru (Kanagawa, JP)

  Assignee(s): Morinaga Milk Industry Co., Ltd. (Tokyo, JP)

  Patent Number: 6,451,584

  Date filed: June 14, 1999

  Abstract: A Lactobacillus bifidus growth promoting composition which significantly grows lactobacillus bifidus and does not produce any side effect such as **diarrhea,** and a blend comprising the above composition and other edible ingredients, and the composition comprises at least one oligosaccharide selected among lactulose, fructo-oligosaccharide, and galacto-oligosaccharide, and raffinose as the active ingredients.

Excerpt(s): The present invention pertains to a composition that can be orally administered to bring intestinal flora to a good state and efficiently control intestinal function, and the use thereof. In further detail, the present invention pertains to a Lactobacillus bifidus growth promoting composition which comprises 1 or 2 or more oligosaccharides selected from lactulose, galacto-oligosaccharide, and fructo-oligosaccharide, and raffinose as the active ingredients, and a blend which comprises the above-mentioned composition and other edible ingredients. Approximately 100 species of microorganisms and 100 trillion or more individual microorganisms live in the human intestines and form the intestinal bacteria plexus. Intestinal bacteria, such as Lactobacillus bifidus and the like, have a strong relationship with the health of humans, and there are bacteria that are considered to have a beneficial effect on the body and bacteria that appear to generate putrefactive substances and carcinogens, etc., and have a detrimental effect on the body. The distribution of these flora varies with factors such as age, race, lifestyle and environment, diet, etc. Intestinal flora in particular are markedly affected by daily diet. Consequently, diet is very important in enhancing a function for controlling intestinal condition. Commercial milk products, such as yogurt, etc., containing Lactobacillus bifidus for balanced intestinal function have been widely used for years. By means of these products, viable lactic acid bacteria are ingested in order to balance intestinal function. On the other hand, it is known that sugar sources are very important for intestinal Lactobacillus bifidus growth and various oligosaccharides that are known as Lactobacillus bifidus growth promoters are now being actively used. These oligosaccharides share in common the fact that they are not broken down by human digestive enzymes, they are not absorbed from the intestines, they are selectively assimilated by Lactobacillus bifidus, etc., and many oligosaccharides, including lactulose, various galacto-oligosaccharides, various fructo-oligosaccharides, isomalto-oligosaccharides, xylo-oligosaccharides, etc., are known.

Web site: http://www.delphion.com/details?pn=US06451584__

- **Method and composition for treatment of infant diarrhea**

  Inventor(s): Andrieux; Claude (Paris, FR), Bouley; Christine (Vaucresson, FR), Guerin-Danan; Corinne (Paris, FR), Postaire; Eric (Vanves, FR)

  Assignee(s): Compagnie Gervais Danone (Levallois-Perret, FR)

  Patent Number: 6,399,055

  Date filed: October 27, 1998

  Abstract: L. casei DN 114-001 is a bacterial agent known for its utility in the fermentation of milk products. A fermented milk product comprising as the sole bacterial agent L. casei DN 114-001 is effective in reducing the number of rotavirus associated **diarrhea** episodes experienced by infants up to 24 months of age. In particular, the number of rotavirus associated **diarrhea** episodes, as well as their severity and duration is reduced in children receiving milk products fermented with L. casei DN 114-001, present in the fermented milk product in amounts of at least 10.sup.6 CFU/g. L. casei may be the sole bacterial agent present in the fermented milk product, and yet effective reduction of **diarrhea** episodes associated with rotavirus infection is obtained.

  Excerpt(s): This invention pertains to a composition comprising an effective amount of a publically available bacterial strain, Lactobacillus casei strain DN 114-001 as an aid to resisting rotavirus infection and **diarrhea** associated therewith, as well as reducing the severity and persistence of rotavirus **diarrhea,** in children up to 24 months of age. The

invention also pertains to a method of supplementing the nutrition of infants up to 24 months of age with a fermented milk product fermented by L. casei DN 114-001 on a daily basis, as a **diarrhea** preventive, and in an effort to reduce frequency, severity and duration of diarrheal episodes. Importantly, L. casei DN 114-001 is effective, alone, as the sole bacterial agent in addressing **diarrhea** in infants up to 24 months of age. Group A rotavirus is the leading cause of **diarrhea** among children aged 6 to 24 months worldwide. Rotavirus associated **diarrhea** causes 870,000 deaths/year principally in developing countries (1). Symptoms are watery **diarrhea,** frequently associated with severe dehydration (2) and malabsorption of nutrients (3, 4). Limited investigations by mucosal biopsy of infected infants have shown that rotavirus principally infects the cells of the small intestine. Introduction of fermented milk products in infant diet has been proposed for the prevention or treatment of acute **diarrhea** (4, 5-10). These products contribute to a well balanced diet and contain lactic acid bacteria (LAB) which are known for their healthful influence, especially in infants (11). Clinical and experimental studies have reported preventive and protective effects of LAB consumption on rotavirus **diarrhea.** Incidence of **diarrhea** and rotavirus shedding have been reduced in infants receiving the bacterial association Streptococcus thermophilus and Bifidobacterium bifidum (12). After oral rehydration, a significant reduction of diarrheal symptoms have been observed when infants consumed Lactobacillus casei strain GG (13-15), Lactobacillus reuteri (15) or a milk fermented by Bifidobacterium longum (16). The mechanisms involved in this protection remain poorly understood. In a previous study, we have developed a germ-free suckling rat model to study group A rotavirus associated **diarrhea** (17). In this model, 5-day old infected rats developed a 6-day **diarrhea** characterized by watery feces containing rotavirus antigens. Histological analyses have demonstrates that rotavirus infects enterocytes and induces cellular vacuolation in the small intestine. Clinical and histopathological analyses were assessed in infected suckling rats supplemented by a milk fermented by the Lactobacillus casei strain DN 114-001, which has been previously involved in a beneficial effect on **diarrhea** in children (18).

Web site: http://www.delphion.com/details?pn=US06399055__

- **Method for preventing diarrhea**

  Inventor(s): Miller; Langdon L. (Lebanon, NJ), O'Dowd; Hugh Michael (Long Valley, NJ), Rothermel; John David (Randolph, NJ)

  Assignee(s): Novartis, A.G. (CH), Pharmacia & Upjohn Co. (IT)

  Patent Number: 6,395,708

  Date filed: August 25, 2000

  Abstract: The present invention relates to a method for preventing irinotecan-induced or camptothecin-induced or camptothecin- analog-induced **diarrhea** by administering an effective amount of octreotide. In particular the invention concerns new methods, combination formulations and kits to prevent late **diarrhea** caused by irinotecan or camptothecin, or camptothecin-analog administration.

  Excerpt(s): The present invention relates to an agent for preventing **diarrhea** and particularly to a pharmaceutical agent for preventing diarrheal symptoms caused by administration of irinotecan or a salt thereof, particularly in the form of its hydrochloride, or attributed to its active metabolite, SN-38. More particularly, the invention concerns new methods, combination formulations and kits to prevent late **diarrhea** induced by irinotecan administration. In the present specification, unless

otherwise specified, the term "irinotecan" includes also pharmaceutically acceptable salts, e.g., the hydrochloride salt, and metabolites, such as, e.g. SN-38. In the present specification, unless otherwise specified, the term "octreotide" includes also pharmaceutically acceptable salts of octreotide, e.g., the acetate. By the term "administered" or "administering" as used herein, is meant standard delivery methods, e.g., parenteral administration, including continuous infusion and intravenous, intramuscular and subcutaneous injections, and oral administration. Diarrhea, characterized by the frequent defecation of liquid or liquid-like stools, often develops as a side effect during clinical treatment with chemotherapeutic agents. This adverse effect is most commonly associated with chemotherapeutic agents such as 5-fluorouracil, cisplatin or irinotecan hydrochloride. In particular, late **diarrhea** due to the administration of irinotecan can be prolonged, may lead to dehydration and electrolyte imbalance and can be, in some cases, sufficiently serious that irinotecan administration must be modified, interrupted or discontinued. **Diarrhea** poses a problematic symptom for patients, and because it may provoke reductions in irinotecan doses or the frequency of irinotecan administration, **diarrhea** may compromise the therapeutic efficacy of irinotecan.

Web site: http://www.delphion.com/details?pn=US06395708__

- **Method of administering camptothecin compounds for the treatment of cancer with reduced side effects**

  Inventor(s): Bouscarel; Bernard (Arlington, VA), Kobayashi; Kumihike (Urawa, JP)

  Assignee(s): The George Washington University (Washington, DC)

  Patent Number: 6,407,117

  Date filed: March 23, 2000

  Abstract: Methods of administering camptothecin compounds such as irinotecan hydrochloride to reduce a **diarrhea** side effect and methods of treating cancer and AIDs with camptothecin compounds including administering the camptothecin compounds while maintaining the intestinal lumen and the bile at an alkaline pH.

  Excerpt(s): The present invention relates to camptothecin compounds, in particular, irinotecan hydrochloride composition formulations, and methods of administering camptothecin compounds such as irinotecan hydrochloride for the treatment of cancer and AIDS, with reduced side effects. Camptothecin is a quinoline-based alkaloid found in the barks of the Chinese Camptotheca tree and the Asian nothapodytes tree. It is a close chemical relative to aminocamptothecin, CPT-11 (irinotecan), DX-8951F and topotecan. These compounds are useful in treating breast cancers, ovarian cancer, colon cancer, malignant melanoma, small cell lung cancer, thyroid cancers, lymphomas and leukemias. These compounds are also used for the treatment of AIDS. Irinotecan hydrochloride (CPT-11) (4S)-4,11-diethyl-4-hydroxy-9-[(4-piperidinopiperidino) carbonyloxy]-1H-pyrano [3',4':6,7] indolizino[1,2-b]quinoline-3,14(4h,12H) dione hydrochloride, has a novel mechanism of antitumor activity, namely the inhibition of DNA topoisomerase I. Topoisomer-ases are the enzymes which wind and unwind the DNA that makes up the chromosomes. As the chromosomes must be unwound to make proteins, camptothecin compounds keep the chromosomes wound tight so that they cannot make proteins. Because cancer cells grow at a much, faster rate than normal cells, they are more vulnerable to topoisomerase inhibition than normal cells.

  Web site: http://www.delphion.com/details?pn=US06407117__

- **Methods and compositions to identify swine genetically resistant to F18 E. coli associated diseases**

  Inventor(s): Bosworth; Brad T. (Littleton, NC), Vogeli; Peter (Zurich, CH)

  Assignee(s): Biotechnology Research & Development Corp. (Peoria, IL), Swiss Federal Institute of Technology (Zurich, CH), The United States of America as represented by the Secretary of Agriculture (Washington, DC)

  Patent Number: 6,596,923

  Date filed: November 19, 1999

  Abstract: The present invention provides non-invasive methods and compositions to differentiate, with a high level of sensitivity and specificity, swine that are genetically susceptible to diseases associated with F18 E. coli infection, from resistant swine. DNA polymorphisms in the swine alpha (1,2) fucosyltransferase 1 (FUT1) gene were used to differentiate resistant from susceptible swine. The invention includes a polypeptide with amino acid substitutions, encoded by the nucleotide polymorphisms, a molecular diagnostic assay, and a kit for the differentiation, of E. coli F18-adhesion resistant, heterozygous (carrier) and homozygous susceptible pigs. The molecular test identifies susceptibility to oedema disease and postweaning **diarrhea** with high sensitivity and specificity, therefore, is useful to swine breeder in their effort to enhance for resistance. Information on the polymorphisms of the present invention provides insight into causation and treatment of E. coli associated intestinal disorders.

  Excerpt(s): Compositions and non-invasive methods are provided for the identification of swine genetically resistant to E. Coli bacteria supplied with fimbriae F18. DNA polymorphisms in the swine alpha (1,2) fucosyltransferase (FUT1) gene were identified that differentiate resistant from susceptible swine and provide a diagnostic test useful for swine breeders. A major problem in breeding swine is to keep them disease-free. Intestinal disorders postweaning are a particular problem. A limited number of serotypes of toxigenic Escherichia (E.) Coli strains are the causative agents of oedema disease and postweaning **diarrhea** in swine which induce serious economic losses, especially among piglets aged 4 to 12 weeks, in swine breeding farms all over the world. The typical symptoms of oedema disease are neurological signs such as ataxia, convulsions and paralysis. At post mortem examination, oedema is typically present at characteristic sites such as eyelids and forehead, stomach wall and mesocolon. The diseases are cause be Shiga-like toxin-II variant and enterotoxins LT, Sta, Stb respectively, produced by E. coli that colonize the surface of the small intestine without effecting major morphological changes of the enterocytes (cells in the intestine). Certain types of bacterial E. coli strains, F18, F4 and K88 are major lethal villains in this regard. "Oedema disease of pigs is an enterotoxaemia characterized by generalized vascular damage. The latter is cause by a toxin, Shiga-like toxin II variant, produced by certain strains of E. coli" (Bertschinger et al., 1993). The E. coli are distinguished by their pili types, a group of adhesive fimbriae that are related are designated e.g., K88 or F18 (Vogeli et al., 1997). Not all swine succumb to E. coli infections. Colonization depends on adherence of the bacteria to the enterocytes which is mediated by the bacterial fimbriae designated e.g., K88 or F18. Susceptibility to adhesion, i.e. expression of receptors in swine for binding the fimbriae, has been shown to be genetically controlled by the host and is inherited as a dominant trait with, in the case of F18, B being the susceptibility allele and b the resistance allele. (Vogeli et al., 1996; Meijerink et al., 1996). The genetic locus for this E. coli F18-receptor (ECF18R) has been mapped to porcine chromosome 6 (SSC6), based on its close genetic linkage to the S locus and other loci of

the halothane (HAL) linkage group on chromosome 6. The receptor for K88 E. coli is on chromosome 13.

Web site: http://www.delphion.com/details?pn=US06596923__

- **Mu-opiate receptor peptides**

  Inventor(s): Hackler; Laszlo (Metairie, LA), Kastin; Abba J. (Metairie, LA), Zadina; James E. (Metairie, LA)

  Assignee(s): Administrators of the Tulane Educational Fund (New Orleans, LA)

  Patent Number: 6,303,578

  Date filed: February 18, 1999

  Abstract: This invention relates to certain peptides and linear and cyclic analogs thereof that bind to the mu (morphine) opiate receptor with higher affinity, selectivity and potency than currently available peptides. This invention also relates to pharmaceutical preparations containing an effective amount of the peptides or salts thereof, and methods for providing analgesia, relief from gastrointestinal disorders such as **diarrhea,** and therapy for drug dependence containing a pharmaceutically effective amount of the peptides.

  Excerpt(s): This invention relates to peptides that bind with high affinity and selectivity to the mu (morphine) opiate receptor; pharmaceutical preparations containing an effective amount of the peptides or salts thereof; and methods for providing analgesia, relief from gastrointestinal disorders such as **diarrhea,** and therapy for drug dependence containing an effective amount of the peptides. Many peptides have been found that exhibit opiate-like activity by binding to opiate receptors. Three different types of opiate receptors have been found: delta (.delta.), kappa (.kappa.) and mu (.mu.). The major putative function for opiates is their role in alleviating pain. Other areas where opiates are well-suited for use in treatment are conditions relating to gastrointestinal disorders, schizophrenia, obesity, blood pressure, convulsions, and seizures. Although the.delta. and.kappa. receptors may also mediate analgesia, activation of.mu. receptors is the primary and most effective means of inducing analgesia, and is the primary mechanism by which morphine acts. To date, opiates, opioid peptides, and analogs thereof, have demonstrated a limited degree of specificity and selectivity for the receptor or receptors to which they may bind. The less selective and specific an opiate may be, the greater the chance that increased side effects from the administration of the material will be observed. When an opiate activates more than one receptor, the biological response profile for each receptor is affected, thereby potentiating a spectrum of side effects which may or may not be adverse. Such adverse side effects include heaviness of the limbs, flush or pale complexion, clogged nasal and sinus passages, dizziness, and depression. Compounds that activate.kappa. receptors frequently induce dysphoria.

  Web site: http://www.delphion.com/details?pn=US06303578__

- **Pharmaceutical compositions of O-desmethyl-N-mono-desmethyl-tramadol**

  Inventor(s): Englberger; Werner (Stolberg, DE), Friderichs; Elmar (Stolberg, DE), Hennies; Hagen-Heinrich (Simmerath, DE), Koegel; Babette (Langerwehe, DE)

  Assignee(s): Gruenenthal GmbH (Aachen, DE)

  Patent Number: 6,593,373

  Date filed: October 12, 2001

  Abstract: A method of producing pharmaceutical compositions using O-desmethyl-N-mono-desmethyl-tramadol for the treatment of pain and various related indications, pharmaceutical compositions containing O-desmethyl-N-mono-desmethyl-tramadol, and a method of treating pain, urinary incontinence, **diarrhea** or pruritus using O-desmethyl-N-mono-desmethyl-tramadol.

  Excerpt(s): This invention relates to the use of O-desmethyl-N-mono-desmethyl-tramadol for the production of pharmaceutical compositions for the treatment of pain and various related indications as well as pharmaceuticals comprising O-desmethyl-N-mono-desmethyl-tramadol. The treatment of pain conditions is of great importance in medicine. There is currently a world-wide need for additional pain therapy. The pressing requirement for a target-oriented treatment of pain conditions which is right for the patient which is to be understood as the successful and satisfactory treatment of pain for the patients is documented in the large number of scientific works which have recently and over the years appeared in the field of applied analgesics or on basic research on nociception. The underlying object of the present invention was to provide a substance useful in the treatment of pain and also related indications, as well as pharmaceutical compositions for such treatment.

  Web site: http://www.delphion.com/details?pn=US06593373__

- **Safe attenuated bovine viral diarrhea viruses for use in pregnant cows**

  Inventor(s): Elbers; Knut (Gau-Algesheim, DE), Meyers; Gregor (Walddorfhaeslach, DE)

  Assignee(s): Boehringer Ingelheim Vetmedica GmbH (Ingelheim, DE)

  Patent Number: 6,610,305

  Date filed: November 6, 2000

  Abstract: This invention relates to the use of specifically attenuated live BVD (bovine viral diarrhea) viruses for the preparation of a vaccine for use in the prevention and/or treatment of BVDV infections in breeding stocks of cattle, pregnant cows and for fetal protection in pregnant cows.

  Excerpt(s): The present invention relates to the use of specifically attenuated live BVD (Bovine Viral Diarrhea) viruses for the preparation of a vaccine for use in the prevention and/or treatment of BVDV infections in breeding stocks of cattle, pregnant cows and for fetal protection in pregnant cows. The invention also relates to a method of treatment and/or prevention of BVDV infections in the above named group of cattle. Bovine Viral **Diarrhea** Virus (BVDV) is the causative agent of BVD and mucosal disease in cattle (Baker, 1987; Moennig and Plagemann, 1992; Thiel et al., 1996). Fetal infection during pregnancy can result in the resorption of the fetus, abortions as well as birth of immunotolerant calves which are persistently infected with BVDV. These calves lack or have very low neutralizing antibody titers and are continuously shedding high amounts of virus. Next to acute or persistently infected bulls these calves are the major source for

virus spreading and are therefore of primary importance in the epidemiology of this disease. The major economical impact of BVD results from high abortion rates, stillbirths, fetal resorption, mummification, congenital malformations, and birth of weak and undersized calves. For a detailed review of the pathogenesis, the article of Moennig and Liess of 1995 should be referred to in its entirety.

Web site: http://www.delphion.com/details?pn=US06610305__

- **Substituted aryl compounds useful as modulators of acetylcholine receptors**

  Inventor(s): McDonald; Ian A. (San Diego, CA), Vernier; Jean-Michel (San Diego, CA)

  Assignee(s): Merck & Co., Inc. (Rahway, NJ)

  Patent Number: 6,316,490

  Date filed: July 8, 1997

  Abstract: In accordance with the present invention, a novel class of substituted aryl compounds (containing ether, ester, amide, ketone or thioether substitution) that promote the release of ligands involved in neurotransmission have been discovered. In a particular aspect, compounds of the present invention are capable of modulating acetylcholine receptors. The compounds of the present invention are capable of displacing one or more acetylcholine receptor ligands, e.g.,.sup.3 H-nicotine, from mammalian neuronal membrane binding sites. Invention compounds may act as agonists, partial agonists, antagonists or allosteric modulators of acetylcholine receptors. Therapeutic indications for compounds with activity as acetylcholine receptors include diseases of the central nervous system such as Alzheimer's disease and other diseases involving memory loss and/or dementia (including AIDS dementia); cognitive dysfunction (including disorders of attention, focus and concentration), disorders of extrapyramidal motor function such as Parkinson's disease, progressive supramuscular palsy, Huntington's disease, Gilles de la Tourette syndrome and tardive dyskinesia; mood and emotional disorders such as depression, anxiety and psychosis; substance abuse including withdrawal symptoms and substitution therapy; neurocrine disorders and dysregulation of food intake, including bulimia and anorexia; disorders of nociception and control of pain; autonomic disorders including dysfimction of gastrointestinal motility and function such as inflammatory bowel disease, irritable bowel syndrome, **diarrhea,** constipation, gastric acid secretion and ulcers; pheochromocytoma, cardiovascular dysfunction including hypertension and cardiac arrhythmias, as well as co-medication uses in surgical applications.

  Excerpt(s): The present invention relates to compounds which potentiate neurotransmission by promoting the release of neurotransmitters such as acetylcholine, dopamine and norepinephrine. More particularly, the present invention relates to compounds that are capable of modulating acetylcholine receptors. Invention compounds are useful, for example, for treatment of dysfunction of the central and autonomic nervous systems (e.g. dementia, cognitive disorders, neurodegenerative disorders, extrapyramidal disorders, convulsive disorders, cardiovascular disorders, endocrine disorders, eating disorders, affective disorders, drug abuse, and the like). In addition, the present invention relates to pharmaceutical compositions containing these compounds, as well as various uses therefor. By modulating neurotransmitter release (including dopamine, norepinephrine, acetylcholine and serotonin) from different brain regions, acetylcholine receptors are involved in the modulation of neuroendocrine function, respiration, mood, motor control and function, focus and attention, concentration, memory and cognition, and the mechanisms of substance abuse. Ligands

for acetylcholine receptors have been demonstrated to have effects on attention, cognition, appetite, substance abuse, memory, extrapyramidal function, cardiovascular function, pain and gastrointestinal motility and function. The distribution of acetylcholine receptors that bind nicotine, i.e., nicotinic acetylcholine receptors, is widespread in the brain, including the basal ganglia, limbic system, cerebral cortex and mid- and hind-brain nuclei. In the periphery, the distribution includes muscle, autonomic ganglia, the gastrointestinal tract and the cardiovascular system. Acetylcholine receptors have been shown to be decreased, inter alia, in the brains of patients suffering from Alzheimer's disease or Parkinson's disease, diseases associated with dementia, motor dysfunction and cognitive impairment. Such correlations between acetylcholine receptors and nervous system disorders suggest that compounds that modulate acetylcholine receptors will have beneficial therapeutic effects for many human nervous system disorders. Thus, there is a continuing need for compounds which have the ability to modulate the activity of acetylcholine receptors. In response to such need, the present invention provides a new family of compounds which modulate acetylcholine receptors.

Web site: http://www.delphion.com/details?pn=US06316490__

- **Substituted indoles and uses thereof**

  Inventor(s): Gluchowski; Charles (Wayne, NJ), Jeon; Yoon T. (Ridgewood, NJ)

  Assignee(s): Synaptic Pharmaceutical Corporation (Paramus, NJ)

  Patent Number: 6,303,643

  Date filed: October 17, 2000

  Abstract: This invention is directed to indole and benzothiazole compounds which are selective for cloned human alpha 2 receptors. This invention is also related to uses of these compounds for any indication where use of an alpha 2 agonist may be appropriate. Specifically, this includes use as analgesic, sedative and anaesthetic agents. In addition, this invention includes using such compounds for lowering intraocular pressure, presbyopia, treating migraine, hypertension, alcohol withdrawal, drug addiction, rheumatoid arthritis, ischemic pain, spasticity, **diarrhea,** nasal decongestion, urinary incontinence as well as for use as cognition enhancers and ocular vasoconstriction agents. The invention further provides a pharmaceutical composition comprising a therapeutically effective amount of the above-defined compounds and a pharmaceutically acceptable carrier.

  Excerpt(s): Alpha adrenergic receptors are plasma membrane receptors which are located in the peripheral and central nervous systems throughout the body. They are members of a diverse family of structurally related receptors which contain seven putative helical domains and transduce signals by coupling to guanine nucleotide binding proteins (G-proteins). These receptors are important for controlling many physiological functions and, thus, have been important targets for drug development during the past 40 years. Examples of alpha adrenergic drugs include clonidine, phenoxybenzamine and prazosin (for treatment of hypertension), naphazoline (for nasal decongestion), medetomidine (for veterinary analgesia), UK-14,304 and p-aminoclonidine (for glaucoma). However, most of these drugs produce undesirable side effects, possibly due to their interactions with other receptor subtypes. For example, clonidine is a well known centrally acting antihypertensive agent. However, it also produces untoward side effects such as analgesia, sedation, bradycardia and dry mouth which may be due to its lack of selectivity at.alpha.sub.2 receptors.alpha.-Adrenergic

receptors were originally proposed to have only two (alpha and beta) subtypes (Berthelsen, S.; Pettinger W. Life Sci., 21, 595 (1977)). However, modern molecular biological and pharmacological techniques have led to the identification of at least 6 subtypes (.alpha.sub.1a,.alpha.sub.1b,.alpha.sub.1c,.alpha.sub.2a,.alpha.sub.2b and.alpha.sub.2c) of the adrenergic receptors (Bylund, D. B., Trends Pharmacol. Sci., 9, 356 (1988)). Among many other therapeutic indications,.alpha.sub.2 receptors are believed to modulate pain and behavioral depression by regulating locus coeruleus firing. In addition,.alpha.sub.2 receptors are well known to be involved in effects on blood pressure, heart rate, vasoconstriction and on glaucoma. However, it is not known which therapeutic indications are controlled by each of these subtypes.

Web site: http://www.delphion.com/details?pn=US06303643__

- **Treatment of C. difficile toxin B associated conditions**

  Inventor(s): Armstrong; Glen D. (Edmonton, CA), Heerze; Louis D. (Edmonton, CA)

  Assignee(s): Synsorb Biotech Inc. (CA)

  Patent Number: 6,358,930

  Date filed: November 4, 1999

  Abstract: This invention relates to prevention and/or treatment of antibiotic associated **diarrhea,** including Clostridium difficile associated **diarrhea** (CDAD), pseudomembranous colitis (PMC) and other conditions associated with C. difficile infection, using oligosaccharide compositions which bind C. difficile toxin B. More specifically, the invention concerns neutralization of C. difficile toxin B associated with such conditions.

  Excerpt(s): This invention relates to treatment of antibiotic associated **diarrhea,** including Clostridium difficile associated **diarrhea** (CDAD) and pseudomembranous colitis (PMC) and other conditions associated with C. difficile infection. More specifically, the invention concerns neutralization of C. difficile toxin B, a cytotoxin associated with CDAD, PMC and other conditions caused by C. difficile. The following references are cited in the application as numbers in brackets ([]) at the relevant portion of the application. 1. Bartlett, J. G., et al., "Antibiotic-associated pseudomembranous colitis due to toxin-producing clostridia", N. Engl. J. Med., 298:531-534 (1978).

  Web site: http://www.delphion.com/details?pn=US06358930__

- **Treatment of diarrhea caused by enteropathogenic Escherichia coli**

  Inventor(s): Armstrong; Glen D. (Edmonton, CA), Yanmaele; Rosa P. (Edmonton, CA)

  Assignee(s): The Governs of the University of Alberta (Edmonton, CA)

  Patent Number: 6,291,435

  Date filed: March 1, 2000

  Abstract: This invention relates to compositions and methods useful to treat **diarrhea,** especially **diarrhea** and related conditions initiated or mediated by enteropathogenic E. coli (EPEC), using oligosaccharide compositions. This invention also relates to compositions and methods to reduce the virulence of an EPEC organism.

Excerpt(s): This invention relates to treatment of **diarrhea,** particularly **diarrhea** caused by enteropathogenic Escherichia coli (EPEC). More specifically, the invention concerns compositions and methods which may be used to prevent EPEC infection or ameliorate symptoms caused by EPEC infection. Enteropathogenic Escherichia coli (EPEC) is a significant cause of **diarrhea** world-wide, with disease occuring most frequently in developing countries [1-3]. In these countries, disease occurs regularly in hospitals and clinics, as well as in the general community. EPEC outbreaks in developed countries, on the other hand, usually consist of sporadic, isolated incidents which are localized to neonatal nurseries of hospitals or day-care centers. Infants less than 6 months of age are most often affected, although EPEC is also capable of causing disease in children and adults. The transmission of EPEC infections is thought to occur primarily by the fecal-oral route as a result of contact with infected individuals or with contaminated surfaces or food. The isolation of EPEC from asymptomatic individuals has led to speculation that some individuals may be carriers who can also spread infection. Clinical symptoms of EPEC infection in children consist of **diarrhea** which varies in duration (days to months) and severity [3,4]. In addition to profuse watery stool, symptoms include dehydration, fever, vomiting and weight loss. In protracted or severe cases, disease is often associated with the delayed growth of children, metabolic acidosis (decrease in blood pH resulting from a loss of bicarbonate [5,6]) and, in extreme cases, death. Adults participating in volunteer studies of EPEC infection displayed symptoms similar to those observed in children, but of shorter duration.

Web site: http://www.delphion.com/details?pn=US06291435__

- **Use of 11-phenyl-dibenzazepine compounds to treat diarrhea or scours**

  Inventor(s): Alper; Seth (Jamaica Plain, MA), Brugnara; Carlo (Newton Highlands, MA), Lencer; Wayne I. (Jamaica Plains, MA)

  Assignee(s): Beth Israel Deaconess Medical Center (Boston, MA), Children's Medical Center Corporation (Boston, MA)

  Patent Number: 6,291,449

  Date filed: September 23, 1998

  Abstract: A method and product for treating and preventing **diarrhea** and scours is provided. The method involves treating a subject who has **diarrhea,** or scours, or is at risk of getting **diarrhea** or scours with an aromatic compound of the invention. The products of the invention are a veterinary preparation of the aromatic compound of the invention and an anti-scours agent, and a pharmaceutical preparation of the aromatic compound of the invention and an anti-diarrheal agent.

  Excerpt(s): The present invention relates to methods and products for reducing chloride secretion using aromatic organic compounds. In particular the invention relates to methods of treating **diarrhea** and scours by administering substituted 11-phenyl-dibenaazepine compounds and analogues thereof. Acute and chronic diarrheas represent a major medical problem in many areas of the world. **Diarrhea** is both a significant factor in malnutrition and the leading cause of death (5,000,000 deaths/year) in children less than five years old. Secretory diarrheas are also a dangerous condition in patients of acquired immunodeficiency syndrome (AIDS) and chronic inflammatory bowel disease (IBD). 16 million travelers to developing countries from industrialized nations every year develop **diarrhea,** with the severity and number of cases of **diarrhea** varying depending on the country and area of travel. The major medical consequences of diarrheal diseases include dehydration, acidosis, death and impaired growth.

Diarrhea in barn animals and pets such as cows, pigs and horses, sheep, goats, cats and dogs, also known as scours, is a major cause of death in these animals. **Diarrhea** can result from any major transition, such as weaning or physical movement. One form of **diarrhea** is characterized by **diarrhea** in response to a bacterial or viral infection and generally occurs within the first few hours of the animal's life.

Web site: http://www.delphion.com/details?pn=US06291449__

- **Use of tropical root crops in effective intervention strategies for treating difficult and complex cases and chronic diseases**

  Inventor(s): Slimak; Karen M. (P.O. Box 2444, Springfield, VA 22152)

  Assignee(s): none reported

  Patent Number: 6,632,461

  Date filed: July 12, 2001

  Abstract: This invention relates to an effective intervention plan. In one aspect, the invention relates to the treatment of various symptoms, conditions or diseases, such as **diarrhea,** constipation, congestion, eczema, asthma, fatigue, muscle weakness, tension and spasms, irritable bowel syndrome, swelling, anxiety, multiple chemical sensitivities, moderate to excessive and moderate to severe symptoms due to food allergies, sensitivities and intolerances, bloating, pain, headaches, leaky gut, hypersensitivity, sleep difficulties, severe under weight, eating disorders, obsessive, compulsive disorders, panic attacks, sensory sensitivities, Alzheimer's disease, acid refulx, irritability, delayed motor skills, delayed social skills, autism, PDD, infantile spasms and seizures by withholding for a period of at least 5 days all foods except for root crops.

  Excerpt(s): This invention relates to an effective dietary intervention plan. In one aspect all food is withheld for a period of at least 5 days, except for tropical root crops. In another aspect the invention relates to the treatment of various symptoms, conditions or diseases such as **diarrhea,** constipation, congestion, eczema, asthma, fatigue, muscle weakness, tension, and spasms, irritable bowel syndrome, swelling, anxiety, multiple chemical sensitivities, moderate to extensive and moderate to severe symptoms due to food allergies, sensitivities, and intolerances, bloating, pain, headaches, leaky gut, hyperactivity, sleeping difficulties, severe underweight, eating disorders, obsessive, compulsive disorders, panic attacks, sensory sensitivities, Alzheimer's disease, acid reflux, irritability, delayed motor skills, delayed social skills, autism, PDD, infantile spasms, seizures by withholding from the patient for a period of at least 5 days all food except for concentrated forms of concentrated tropical root crops. Preferably the patient is also removed from external environmental sources of allergens. After the initial withholding period new foods may be introduced according to a particular selection and schedule. In another aspect of the invention the subject undergoes an effective dietary intervention plan in which at least five (5) tropical root crops are selected, each eaten on a successive day, along with selected other meat, vegetables, and oils that the subject has never eaten before, eating a different selection of meat, vegetables, and oils each from different food families each day, with no food or food family being repeated for at least 5 days. In another aspect the invention relates to the treatment of various symptoms, conditions or diseases such as **Diarrhea,** constipation, congestion, eczema, asthma, fatigue, muscle weakness, tension, and spasms, irritable bowel syndrome, swelling, anxiety, multiple chemical sensitivities, moderate to extensive and moderate to severe symptoms due to food allergies, sensitivities, and intolerances, bloating, pain, headaches, leaky gut, hyperactivity, sleeping difficulties, severe underweight, eating

disorders, obsessive, compulsive disorders, panic attacks, sensory sensitivities, Alzheimer's disease, acid reflux, irritability, delayed motor skills, delayed social skills, autism, PDD, infantile spasms, seizures by withholding from the patient for a period of at least 5 days all food except for concentrated forms of concentrated tropical root crops. Preferably the patient is also removed from external environmental sources of allergens. After the initial withholding period new foods may be introduced according to a particular selection and schedule. In another aspect of the invention the subject undergoes an effective dietary intervention plan in which at least seven (7) tropical root crops are selected, each eaten on a successive day, along with selected other meat, vegetables, and oils that the subject has never eaten before, eating a different selection of meat, vegetables, and oils each from different food families each day, with no food or food family being repeated for at least 7 days. In another aspect the invention relates to the treatment of various symptoms, conditions or diseases such as **Diarrhea,** constipation, congestion, eczema, asthma, fatigue, muscle weakness, tension, and spasms, irritable bowel syndrome, swelling, anxiety, multiple chemical sensitivities, moderate to extensive and moderate to severe symptoms due to food allergies, sensitivities, and intolerances, bloating, pain, headaches, leaky gut, hyperactivity, sleeping difficulties, severe underweight, eating disorders, obsessive, compulsive disorders, panic attacks, sensory sensitivities, Alzheimer's disease, acid reflux, irritability, delayed motor skills, delayed social skills, autism, PDD, infantile spasms, seizures by withholding from the patient for a period of at least 5 days all food except for concentrated forms of concentrated tropical root crops. Preferably the patient is also removed from external environmental sources of allergens. After the initial withholding period new foods may be introduced according to a particular selection and schedule.

Web site: http://www.delphion.com/details?pn=US06632461__

- **Vaccine**

  Inventor(s): Brownlie; John (Compton, GB), Clarke; Michael Cyril (Compton, GB), Howard; John Christopher (Compton, GB)

  Assignee(s): Vericore Limited (Lancaster, GB)

  Patent Number: 6,416,764

  Date filed: June 23, 1999

  Abstract: A vaccine comprises a non-cytopathogenic strain of bovine viral **diarrhea** virus, grown in a bovine derived cell line such as MDBK and killed, for example with.beta.-propiolactone. The adjuvant is Quil A.

  Excerpt(s): Bovine virus diarrhoea virus (BVDV) is extremely common in cattle in the UK, the remainder of Western Europe, North America, Australia and Africa. Infection with this virus may result in a variety of syndromes and pathologies influenced largely by the age of animals when first infected. In young, previously uninfected calves the virus causes a transient infection. This is associated with leucopenia, and an interrelated period of immunosuppressive and increased susceptibility to infection with other microorganisms. BVDV is, after RSV (respiratory syncitial virus), probably the most important virus associated with outbreaks of respiratory disease in young housed calves and because of its immuno-suppressive effect it may be involved in other calf infections, for example enteritis. This virus is also considered to be a major contributor to disease in "feedlot calves" in the USA and Canada. Following recovery, animals exhibit a degree of immunity to reinfection. However, this immunity appears not to be absolute or lifelong. More serious problems result from infection of pregnant cattle. Abortion may ensure or

alternatively deformities may be produced in the foetus that is carried to term; these deformities may result from exposure to virus at the time when immunocompetence is developing and could be the result of an incomplete immune response. Infection of the feotus before immunocompetence develops can result in the foetus remaining viraemic through the period of gestation and the subsequent birth of a calf that remains persistently viraemic, with a non-cytopathogenic form of the virus, and specifically immunotolerant to BVDV for life. Such calves are the animals that die later of mucosal disease; an event triggered by superinfection with a cytopathogenic variant of BVDV. It has been estimated that about 0.4% of apparently normal beef calves in the UK are viraemic and these animals represent a major source of infection on farms.

Web site: http://www.delphion.com/details?pn=US06416764__

Patent Applications on Diarrhea

As of December 2000, U.S. patent applications are open to public viewing.[10] 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 diarrhea:

- **3-(diarylmethylene)-8-azabicyclo[3.2.1]octane derivatives**

  Inventor(s): Boyd, Robert E.; (Horsham, PA), Carson, John R.; (Norristown, PA), Coats, Steven J.; (Quakertown, PA), Neilson, Lou Anne; (Sellersville, PA), Pitis, Philip M.; (North Wales, PA), Wu, Wu-Nan; (Lansdale, PA)

  Correspondence: Audley A. Ciamporcero JR.; Johnson & Johnson; One Johnson & Johnson Plaza; New Brunswick; NJ; 08933-7003; US

  Patent Application Number: 20020115662

  Date filed: February 22, 2001

  Abstract: This invention is directed to 3-(diarylmethylene)-8-azabicyclo[3.2.1]octan- e derivatives useful as.delta.-opioid or.mu.-opioid receptor modulators. Depending on their agonist or antagonist effect, the compounds are useful analgesics, immunosuppressants, antiinflammatory agents, agents for the treatment of neurological and psychiatric conditions, medicaments for drug and alcohol abuse, agents for treating gastritis and **diarrhea,** cardiovascular agents and agents for the treatment of respiratory diseases.

  Excerpt(s): The present invention is directed to compounds useful as delta-opioid and mu-opioid receptor modulators. More particularly, the present invention is directed to 3-(diarylmethylene)-8-azabicyclo[3.2.1]o- ctane derivatives useful as delta-opioid or mu-opioid receptor modulators. wherein R is hydrogen, methyl, propyl, hexyl, 2-ethylbutyl, allyl, 3,3-dimethallyl, cyclohexylmethyl, phenethyl, phenylpropyl, 2,2-diphenylethyl, 3,4-dimethoxyphenethyl, 4-fluorophenethyl, 2-furylmethyl, 3,4-methylenedioxybenzyl, cyano and X is N,N-dimethylamino, N,N-diethylamino, N,N-dipropylamino, N-methyl-N-ethylamino, N-methyl-N-propylamino, N-methyl-N-phenylamino, N-ethyl-N-(4-methyl)benzylamino, N-butyl-N-ethylamino, N-butyl-N-propylamino, [N-ethyl-N-(2-methyl)allyl]amino, hydroxy, O-t-butyl and 1-pyrrolidinyl; and, Y is hydrogen, methoxy and methylthio. Other selective 4-[(8-alkyl-8-azabicyclo[3.2.1] octyl-3-yl)-3-arylanilino]-

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

N,N-diethylbenzamide.delta.-opioid ligands have also been described (Thomas, J. B., Atkinson, R. N., Rothman, R. B., Burgess, J. P., Mascarella, S. W., Dersch, C. M., Xu, H. and Carroll, F. I., Biorg. Med. Chem. Lett., 2000, 10: 1281-1284).

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

- **5-ASA derivatives having anti-inflammatory and antibiotic activity and methods of treating diseases therewith**

  Inventor(s): Ekwuribe, Nnochiri Nkem; (Cary, NC), Malson, Elizabeth; (Burbank, CA), Riggs-Sauthier, Jennifer A.; (Raleigh, NC)

  Correspondence: Myers Bigel Sibley & Sajovec; PO Box 37428; Raleigh; NC; 27627; US

  Patent Application Number: 20020111334

  Date filed: August 29, 2001

  Abstract: Compounds are disclosed represented by the following formula: 1where R.sup.1 is a substituted or unsubstituted phenyl group, and where Z is selected such that a compound, Z--R.sup.1--NH.sub.2, formed by cleavage of the azo bond is a non-absorbable antibiotic; or an ester or pharmacologically acceptable salt of the compound of Formula I. Compounds of the present invention may be utilized for the prophylaxis or treatment of various diseases including, but not limited to, intestinal diseases such as inflammatory bowel disease and/or traveler's **diarrhea,** liver diseases such as hepatic encephalopathy, and/or diseases treatable by a non-absorbable antibiotic.

  Excerpt(s): This application claims the benefit of U.S. Provisional Application No. 60/228,682, filed Aug. 29, 2000, the disclosure of which is incorporated herein by reference in its entirety. The present invention relates to 5-ASA derivatives and methods of treating diseases therewith. Many people suffer from inflammatory bowel disease (IBD). IBD is a generic term used to refer to two inflammatory diseases, ulcerative colitis and Crohn's disease. Ulcerative colitis is a chronic inflammatory disease of unknown etiology that affects various portions of the gastrointestinal (GI) tract, particularly the lower GI tract, and more particularly the colon and/or rectum. Crohn's disease is a serious inflammatory disease of the GI tract. It predominates in the intestine (ileum) and the large intestine (colon). Various medications are being used to treat inflammatory bowel disease.

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

- **A2B adenosine receptor antagonists**

  Inventor(s): Palle, Venkata; (Sunnyvale, CA), Varkhedkar, Vaibhav; (Mountain View, CA), Xiao, Dengming; (Longmont, CO), Zablocki, Jeff; (Mountain View, CA)

  Correspondence: Brian Lewis; CV Therapeutics, INC.; 3172 Porter Drive; Palo Alto; CA; 94304; US

  Patent Application Number: 20030064999

  Date filed: June 27, 2002

  Abstract: Disclosed are novel compounds that are A.sub.2B adenosine receptor antagonists, useful for treating various disease states, in particular asthma and **diarrhea.**

Excerpt(s): This Patent Application claims the benefit under 35 U.S.C. 119(e) of U.S. provisional application Serial No. 60/302,208, filed Jun. 29, 2001, the entire disclosure of which is incorporated by reference. The present invention relates to novel compounds that are A.sub.2B adenosine receptor antagonists, and to their use in treating mammals for various disease states, such as gastrointestinal disorders, immunological disorders, neurological disorders, and cardiovascutlar diseases due to both cellular hyperproliferation and apoptosis, and the like. The invention also relates to methods for the preparation of such compounds, and to pharmaceutical compositions containing them. Adenosine is a naturally occurring nucleoside, which exerts its biological effects by interacting with a family of adenosine receptors known as A.sub.1, A.sub.2a, A.sub.2b, and A.sub.3, all of which modulate important physiological processes. For example, A.sub.1 adenosine receptor agonists modulate the cardiostimulatory effects of catecholamine, thus slowing the heart rate, and also prolong impulse propagation through the AV node. Thus, stimulation of A.sub.1 receptors provides a method of treating supraventricular tachycardias, including termination of nodal re-entrant tachycardias, and control of ventricular rate during atrial fibrillation and flutter. A.sub.2A adenosine receptors modulate coronary vasodilation, A.sub.2B receptors have been implicated in mast cell activation, asthma, vasodilation, regulation of cell growth, intestinal function, and modulation of neurosecretion (See Adenosine A.sub.2B Receptors as Therapeutic Targets, Drug Dev Res 45:198; Feoktistov et al., Trends Pharmacol Sci 19:148-153), and A.sub.3 adenosine receptors modulate cell proliferation processes.

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

- **Active compounds of Bao-Ji-Wan for anti-diarrhea and relieving gastrointestinal symptoms**

  Inventor(s): But, Paul Pui-Hay; (Tai Po, HK), Chan, Hsiao Chang; (Shatin, HK), Chung, Yiu Wa; (Ma On Shan, HK), Song, Jing Mei; (Richmond, VA)

  Correspondence: Townsend And Townsend And Crew, Llp; Two Embarcadero Center; Eighth Floor; San Francisco; CA; 94111-3834; US

  Patent Application Number: 20030152657

  Date filed: December 6, 2002

  Abstract: The invention provides methods for treating medical conditions caused by abnormal chloride ion flux with compositions containing active ingredients isolated from the traditional Chinese medicine Bao-Ji-Wan (BJW). The compositions comprise any one, two, or three of the following: magnolol, honokiol, imperatorin, isoimperatorin or only magnolol, honokiol, imperatorin, isoimperatorin and a physiologically acceptable carrier. In preferred embodiments, the medical conditions include disorders of the gastrointestinal tract, such as **diarrhea** and constipation.

  Excerpt(s): The present application claims priority to U.S. Ser. No. 60/339,752, filed Dec. 17, 2001, herein incorporated by reference in its entirety. Not applicable. This invention relates to methods of using pharmaceutical compositions containing active ingredients of the traditional Chinese medicine Bao-Ji-Wan (BJW) for treatment of conditions with abnormal chloride ion flux. In particular, the present invention is directed towards gastrointestinal conditions like **diarrhea** and constipation.

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

- **Animal feed containing simple polysaccharides**

  Inventor(s): Kim, Chulho; (Taejeon, KR), Rhee, Sangki; (Seoul, KR), Song, Kibang; (Taejeon, KR), Yoon, Byoungdae; (Taejeon, KR)

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

  Patent Application Number: 20030086959

  Date filed: July 3, 2002

  Abstract: The present invention relates to an animal feed containing the 0.04-2 (w/w) % simple polysaccharide on the basis of solid powder. The animal feed according to this invention is effective in improving the condition of evacuation, preventing the **diarrhea** and promoting the growth of animals.

  Excerpt(s): Stress on animals, caused by changes in weaning food, animal feed or breeding environment, is often the reason of their **diarrhea** or fluid stool and their retarded growth. Particularly, young domestic animals in the weaning stage are sensitive to change of the environment, and prone to stress and **diarrhea** therefrom. This condition influences a total period of their growth, resulting in extension of the growth period and increase of the breeding cost. In order to prevent and treat **diarrhea** or fluid stool causing an economic loss of livestock farms, several antibiotics, microorganism (Lactobacillus or Bifidobacterium), or oligosaccharide, disclosed in prior art (KR Open Publication No. 90-17493, KR Publication No. 95-4426, JP Publication No. 79-15829, KR Publication No. 94-957, KR Patent No. 171,246, and KR Patent No. 198,727), have been administered. However, in case of a long-term use of these antibiotics, its tolerance to antibiotics may be developed, beneficial intestinal cells in the animal also may be destroyed, and some control of the shipping time of the animal is needed because of the antibiotics' remains in the animal.

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

- **Animal model for flaviviridae infection**

  Inventor(s): Dubovi, Edward J.; (Ithaca, NY), Jacob, James R.; (Cortland, NY), Tennant, Bud C.; (Ithaca, NY)

  Correspondence: Sherry M. Knowles, ESQ.; King & Spalding; 45th Floor; 191 Peachtree Street, N.E.; Atlanta; GA; 30303; US

  Patent Application Number: 20030037353

  Date filed: December 3, 2001

  Abstract: The present invention is a woodchuck or an isolated woodchuck cell infected with bovine viral **diarrhea** virus. The invention can be used to identify new compounds for the treatment of flavivirus, pestivirus or hepatitis C infection using these models.

  Excerpt(s): This invention claims priority to U.S. provisional application No. 60/250,638 filed Dec. 1, 2000. This invention is a woodchuck or woodchuck cell infected with a bovine viral **diarrhea** virus and their use as models of Flaviviridae infection. Infection with hepatitis C virus (HCV) has a major medical impact worldwide leading to chronic infections, cirrhosis of the liver and cancer (Di Bisceglie, A. M., and Bacon, B. R. (1999) Scientific American (Oct.): 80-85). Worldwide over 100 million people are chronically infected (Alter, M. J. (1997) Hepatology, 26(suppl. 1): 62S-65S; Hoofnagle, J. H., and DiBisceglie, A. M. (1997) New Engl. J. Med., 336: 337-356). In the U.S. almost 4 million

people are chronically infected, and almost 9,000 people die annually from the disease (Chisari, F. V., and Ferrari, C. (1997) Viral hepatitis. In: Viral Pathogenesis. Ed: Nathanson, N., et al. Lippincott-Raven Publishers, Philadelphia, 1997: 745-778). The chimpanzee (Pan troglodites) is the only animal model with which to study the pathogenesis of hepatitis C virus (HCV) infection of humans (Houghton, M. Hepatitis C Viruses. In: Fields Virology, third edition. Eds; Fields, B. H., Knipe, D. M., Howley, P. M., et al. Lippencott-Raven Publishers, Philadelphia, 1996: 1035-1058).

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

- **Anti-diarrheal and method for using the same**

  Inventor(s): Adalsteinsson, Orn; (Kennett Square, PA), Brodie, David A.; (East Windsor, NJ), Greenblatt, Hellen Chaya; (Wilmington, DE), Jacoby, Henry; (Brigantine, NJ)

  Correspondence: Basil S. Kirkelis; Arkion Life Sciences; 3521 Silverside Road; Quillen Building; Wilmington; DE; 19810; US

  Patent Application Number: 20030068314

  Date filed: January 22, 2002

  Abstract: A food product and method for treating and preventing **diarrhea** in a subject animal suffering from or susceptible to **diarrhea.** The method comprises administering an egg product to the subject animal wherein the egg product is obtained from a hyperimmunized avian.

  Excerpt(s): This application is a Continuation-in-Part of Provisional Application Serial No. 60/084,765, filed May 8, 1998, now abandoned and U.S. application Ser. No. 09/291,784, filed Apr. 14, 1999, now abandoned. This invention relates to a product and method for treating and preventing **diarrhea** and diarrheal symptoms. More particularly, this invention relates to a natural food product which, when administered to a subject animal, treats and prevents **diarrhea** and diarrheal symptoms in that subject animal. Diarrhea is a worldwide problem for individuals of all ages. **Diarrhea** is a common condition, which at the very least is life disrupting and can be life threatening. Acute **diarrhea** can be produced by a variety of pathological organisms, functional disruptions of intestinal function and as a drug-related side effect.

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

- **Benzamidine derivatives**

  Inventor(s): Baxter, Ellen W.; (Glenside, PA), Nortey, Samuel O.; (Elkins Park, PA), Reitz, Allen B.; (Lansdale, PA)

  Correspondence: Audley A. Ciamporcero JR.; Johnson & Johnson; One Johnson & Johnson Plaza; New Brunswick; NJ; 08933-7003; US

  Patent Application Number: 20020123489

  Date filed: December 11, 2001

  Abstract: Benzamidine derivatives are useful delta-opioid receptor modulators, agonists useful as analgesics and antagonists useful as immunosuppressants, antiinflammatory agents, agents for the treatment of neurological and psychiatric conditions, medicaments for drug and alcohol abuse, agents for treating gastritis and **diarrhea,** cardiovascular agents and agents for the treatment of respiratory diseases.

Excerpt(s): The present invention is directed to delta-opioid receptor modulators and methods for use thereof. More particularly, the present invention is directed to benzamidine derivatives which are delta-opioid receptor agonists or antagonists and methods for use thereof. The foregoing reference compounds have been described as either.delta.-opioid or.mu.-opioid receptor agonists or antagonists. wherein R and R' are hydrogen, lower alkyl, hydroxy, lower alkoxy, halogen or trifluoromethyl and may be the same or different; R" is lower alkyl, lower alkenyl, cycloalkyl, or phenyl, and R'" is hydrogen, lower alkyl, lower alkenyl, carboalkoxy, carboalkoxyalkyl, formyl, phenyl, halophenyl, cinnamyl, benzyl or benzhydryl as having hypoglycemic activity. The lower alkyl, lower alkoxy and lower alkenyl groups may be branched or straight chained and contain up to 6 carbon atoms. The cycloalkyl groups contain from 3 to 7 carbon atoms in the ring which may also carry a lower alkyl substituent. The carboalkoxy groups contain alkyl groups having from 1 to 5 carbon atoms and include carbomethoxy, carbethoxy, carbopropoxy, carbobutoxy and the like. Desirably, R and R' are lower alkyl, preferably methyl, or halogen, preferably chloro; R may be hydrogen and R' is then chloro, lower alkyl, preferably methyl, or trifluoromethyl; R" is lower alkyl, preferably isobutyl, and R'" is carbethoxy. Exemplified compounds include those wherein R is selected from hydrogen, chlorine, fluorine or methyl; R' is selected from hydrogen, chlorine, fluorine, methyl, methoxy, hydroxy or trifluoromethyl; R" is selected from hydrogen, chlorine, fluorine, methyl, ethyl, n-propyl, n-butyl, i-butyl, i-amyl, n-hexyl, allyl, cyclohexyl, phenyl or 3,4-dimethylphenyl; R'" is selected from hydrogen, methyl, ethyl, n-hexyl, allyl, phenyl, 4-Cl-phenyl, benzhydryl, benzyl, 2,4-Cl.sub.2-benzyl, 2,3,4-(MeO).sub.3-benzyl, COOEt or CHO.

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

- **Benzimidazoles and benzothiazoles and uses thereof**

Inventor(s): Gluchowski, Charles; (Wayne, NJ), Jeon, Yoon T.; (Ridgewood, NJ)

Correspondence: John P. White; Cooper & Dunham Llp; 1185 Avenue OF The Americas; New York; NY; 10036; US

Patent Application Number: 20030105147

Date filed: October 22, 2002

Abstract: This invention is directed to novel indole and benzothiazole compounds which are selective for cloned human alpha 2 receptors. This invention is also related to uses of these compounds for any indication where use of an alpha 2 agonist may be appropriate. specifically, this includes use as analgesic, sedative and anaesthetic agents. In addition, this invention includes using such compounds for lowering intraocular pressure, presbyopia, treating migraine, hypertension, alcohol withdrawal, drug addiction, rheumatoid arthritis, ischemic pain, spasticity, **diarrhea,** nasal decongestion, urinary incontinence as well as for use as cognition enhancers and ocular vasoconstriction agents. The invention further provides a pharmaceutical composition comprising a therapeutically effective amount of the above-defined compounds and a pharmaceutically acceptable carrier.

Excerpt(s): Throughout this application, various references are referred to within parentheses. Disclosures of these publications in their entireties are hereby incorporated by reference into this application to describe more fully the state of the art to which this invention pertains. Alpha adrenergic receptors are plasma membrane receptors which are located in the peripheral and central nervous systems throughout the body. They are members of a diverse family of structurally related receptors which contain seven

putative helical domains and transduce signals by coupling to guanine nucleotide binding proteins (G-proteins). These receptors are important for controlling many physiological functions and, thus, have been important targets for drug development during the past 40 years. Examples of alpha adrenergic drugs include clonidine, phenoxybenzamine and prazosin (for treatment of hypertension), naphazoline (for nasal decongestion), medetomidine (for veterinary analgesia), UK-14,304 and p-aminoclonidine (for glaucoma). However, most of these drugs produce undesirable side effects, possibly due to their interactions with other receptor subtypes. For example, clonidine is a well known centrally acting antihypertensive agent. However, it also produces untoward side effects such as analgesia, sedation, bradycardia and dry mouth which may be due to its lack of selectivity at.alpha.sub.2 receptors.alpha.-Adrenergic receptors were originally proposed to have only two (alpha and beta) subtypes (Berthelsen, S.; Pettinger W. Life Sci., 21, 595 (1977)). However, modern molecular biological and pharmacological techniques have led to the identification of at least 6 subtypes (.alpha.sub.1a,.alpha.sub.1b,.alpha.sub.1c,.alpha.sub.2a,.alpha.sub.2b and.alpha.sub.2c) of the adrenergic receptors (Bylund, D. B., Trends Pharmacol. Sci., 9, 356 (1988)).

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

- **Bvdv virus-like particles**

  Inventor(s): Rijsewijk, Franciscus Antonius Maria; (Lelystad, NL), Schlapp, Tobias; (Koln, DE)

  Correspondence: Jeffrey M. Greenman; Vice President, Patents And Licensing; Bayer Corporation; 400 Morgan Lane; West Haven; CT; 06516; US

  Patent Application Number: 20030129744

  Date filed: December 20, 2002

  Excerpt(s): The present invention relates to bovine viral **diarrhea** virus (BVDV) virus-like particles, a polycistronic RNA and DNA corresponding thereto encoding a polyprotein of BVDV structural proteins that are sufficient to form BVDV virus-like particles, a viral vector encoding factors and structural proteins for the assembly of BVDV virus-like particles, a vaccine comprising BVDV virus-like particles, a diagnostic kit and methods for preparing BVDV virus-like particles. Bovine viral **diarrhea** virus (BVDV) is the etiological agent of bovine viral **diarrhea** in cattle and has a world wide distribution and a prevalence that can be as high as 90%. BVDV is a member of the genus pestivirus of the Flaviviridae family [Horzinek (1991), Pestiviruses--taxonomic perspectives, Arch. Virology Suppl. 3, 55-65]. BVDV has a positive-stranded RNA genome of approximately 12.5 kilo bases kb), coding for one open reading frame which can be translated into one large polyprotein [Collet et al. (1988), Proteins encoded by bovine viral **diarrhea** virus: the genomic organisation of a pestivirus, Virology 165, 200-208]. A BVDV virion consists of a genomic RNA fitted into a nucleocapsid which is surrounded by an envelope containing glycoproteins.

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

- **Composition and method to prevent or reduce diarrhea and steatorrhea in HIV patients**

  Inventor(s): Das, Simantini; (Easton, PA), Sipos, Tibor; (Lebanon, NJ), Wignot, Teresa Marie; (Dallas, PA)

  Correspondence: Law Office OF Imre Balogh; 276 Smith School Road; Perkasie; PA; 18944; US

  Patent Application Number: 20030180279

  Date filed: March 19, 2002

  Abstract: Method of preventing or reducing **diarrhea** and/or steatorrhea in HIV-positive patients being treated with High Activity Antiretroviral drugs containing protease inhibitors, nucleoside reverse transcriptase inhibitors or non-nucleoside reverse transcriptase inhibitors. The method includes the steps of: administering to the HIV-positive patient a High Activity Antiretroviral drug containing a protease inhibitor, a nucleoside reverse transcriptase inhibitor or a non-nucleoside reverse transcriptase inhibitor; and co-administering with the HAART drug a gastric acid-resistant polymer-coated and buffered digestive enzyme composition containing pancreatic proteases, lipases, co-lipases, nucleases, amylases and other bio-active substances produced by the pancreatic gland.

  Excerpt(s): The present invention relates to a composition and method using the composition to treat and to prevent/reduce **diarrhea** and steatorrhea in HIV patients who are treated with High Activity Antiretroviral Therapy, hereinafter referred to as "HAART". The current most effective treatment of individuals infected with Human Immunodeficiency Virus, hereinafter referred to as "HIV", is the HAART method which comprises administering a combination of drugs that attack the HIV mechanism for viral reproduction. The therapy consists of using drugs that inhibit reverse transcriptase and HIV protease. HAART is intended to increase CD4 lymphocyte counts and suppression of HIV load in response to the antiretroviral therapy. Ultimately, the therapy results in declining HIV-related morbidity and mortality. Drugs used in HAART include: protease inhibitors (PI); non-nucleoside reverse transcriptase inhibitors (NNRTI); and nucleoside reverse transcriptase inhibitors (NRTI). Table I lists these drugs by trade name, chemical name and type.

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

- **Compositions and methods for treating diarrhea**

  Inventor(s): Shushunov, Sergei; (Glencoe, IL)

  Correspondence: Joseph A. Mahoney,; Mayer, Brown & Platt; P.O. Box 2828; Chicago; IL; 60690; US

  Patent Application Number: 20030143293

  Date filed: January 31, 2002

  Abstract: This invention relates to compositions, methods, combinations, and kits for treating, preventing, or reducing the risk of developing **diarrhea** in a mammal; or treating, preventing, or reducing the risk of developing a symptom associated with, or related to, **diarrhea** in a mammal. In particular, the compositions, methods, combinations, and kits comprise an anti-diarrheal agent and an electrolyte.

Excerpt(s): Acute and chronic **diarrhea** represent a major medical problem in many areas of the world. The major medical consequences of diarrheal diseases include dehydration, acidosis, impaired growth, malnutrition, and death. Although the major consequences of diarrheal diseases are very similar, there are numerous causes of **diarrhea.** Secretory and exudative **diarrhea** are primarily caused by bacterial or viral infections. The most common diarrheal causing bacteria is enterotoxogenic E-coli having the K99 pilus antigen. Common viral causes of **diarrhea** include rotavirus and coronavirus. Other infectious agents that cause **diarrhea** include adenovirus, cryptosporidium, shigella, cholera, vibrio bacteria, giardia lamblia, and salmonella, among others. Rotaviruses have been estimated to cause 30-50% of all cases of severe diarrheal disease in humans.

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

- **Compositions for preventing and treating digestive organs diseases**

Inventor(s): Araki, Hiromasa; (Yamatokoriyama-shi, JP), Kakehi, Kazuaki; (Nara-shi, JP), Kawabata, Atsufumi; (Yamatotakada-shi, JP), Kawai, Kenzo; (Matsubara-shi, JP), Kuroda, Ryotaro; (Osaka-shi, JP), Nishikawa, Hiroyuki; (Kashiba-shi, JP), Nishimura, Sachiyo; (Sakurai-shi, JP), Tanaka, Shuichi; (Sennan-gun, JP)

Correspondence: Browdy And Neimark, P.L.L.C.; 624 Ninth Street, NW; Suite 300; Washington; DC; 20001-5303; US

Patent Application Number: 20030166553

Date filed: August 22, 2002

Abstract: The present invention provides a composition for safely and effectively preventing and treating digestive organs diseases, particularly, gastric ulcer, duodenal ulcer, gastritis, **diarrhea,** enteritis and the like. There is also provided a composition having a novel mechanism of action in order to solve the problems which was difficult to be solved by the side effect previously known mechanisms of action. More particularly, there is provided a pharmaceutical composition containing an ingredient which activates PAR-2 as an essential ingredient, which is useful for inhibiting gastric acid secretion, promoting digestive tract mucus secretion, protecting digestive tract mucosa, repairing tissue of digestive organs, and preventing and treating digestive organs diseases.

Excerpt(s): The present invention relates to compositions for preventing and treating digestive organs diseases, especially, compositions for preventing and/or treating gastric ulcer, duodenal ulcer, gastritis, **diarrhea,** enteritis and the like. Peptic ulcer such as gastric ulcer, duodenal ulcer and the like are resulted from the disruption of a balance between aggressive factors and protective factors. Example of disruption-inducing factors include drugs (e.g., non-steroidal anti-inflammatory agents, adrenocortical hormone agents, antibiotics, anti-cancer agents, oral hypoglycemic agents), stress, alcohols, corrosive drugs, cirrhosis, anisakid spp., eating habits and the like. At present, aggressive factor inhibitors, protective factor enhancers, and combinations thereof are clinically used. As the aggressive factor inhibitors, there are clinically used antacids (e.g., sodium bicarbonate and aluminum hydroxide gel, magnesium oxide etc.), anticholinergics (e.g., atropine sulfate, pirenzepine hydrochloride etc.), H2-receptor antagonists (e.g., cimetidine, ranitidine, famotidine, nizatidine, roxatidine etc.), proton pump inhibitors (e.g., omepurazor, ransoprazol, ransoprazol sodium etc.), anti-gastrin drugs (e.g., proglumide, secretin, urogastorone), and anti-pepsin drugs (sucrose sulfate ester, sucralfate etc.) and the like.

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

- **Compositions of alpha3beta4 receptor antagonists and opioid agonist analgesics**

  Inventor(s): Simon, David Lew; (Mansfield Center, CT)

  Correspondence: David L. Simon, M.D.; P.O. Box 618; Mansfield Center; CT; 06250; US

  Patent Application Number: 20030199439

  Date filed: April 22, 2002

  Abstract: A pharmaceutical composition comprising an opioid agonist analgesic and an.alpha.3.beta.4 nicotinic receptor antagonist effective to separate the brain-derived wanting of the opioid from the analgesic or anti-diarrhea effect of the opioid agonist.

  Excerpt(s): This invention relates to pharmaceutical compositions, specifically to those containing opioid agonist analgesics as at least one component of the composition. Opioid agonist analgesics have long been a cornerstone of pharmaceutical management of pain and other medical maladies such as loose stool or **diarrhea.** However, use of opioid agonist analgesics may be accompanied by feeling euphoria as a reaction apart from relief of pain, or may be accompanied by other pharmaceutical effects as to create a wanting of the opioid agonist analgesic as an issue separate and distinct from the issue of pain relief. It is undesirable for a human patient to want to be administered an opioid agonist analgesic for reasons other than relief of pain or prescribed treatment of licit medical maladies such as loose stool. Such a wanting could result in the opioid agonist analgesic being administered in quantities greater than that required to treat pain and other licit medical maladies, which would result in waste of opioid agonist analgesic, and an increase in spending for opioid agonist analgesics. This is of great societal significance in managing the allocation of scarce resources available in the treating health care system in general. Any wastage of money on a pharmaceutical or medication results in less money available for other needed resources, be they other medications or health care services. In and of itself, a decrease in wanting of opioids apart from pain relief and other licit uses (hereafter "any licit use") would be of great of great utility, whether it be in an opioid naive individual (i.e., one that has not been previously exposed to opioid analgesics) or an individually chronically exposed to opioid agonist analgesics (e.g., a chronic pain patient, as one who is long suffering from malignant or cancer-related pain). There have been attempts to reduce the effective amount of opioid agonist analgesic for any licit use. Such attempts have included the co-administration of opioids with NMDA-receptor antagonists or relatively low doses of opioid antagonist. These methods, if effective, could theoretically serve the desired purpose of reducing wastage of opioids, however these methods have not been demonstrated to decrease the wanting of the opioid apart from any licit use, and in fact, could theoretically potentiate the opioid agonist effect to possibly increase the wanting desire of the opioid agonist analgesic, which would have the opposite of the desired effect to decrease wastage and optimize management of scare health care resources.

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

- **Compositions to identify swine genetically resistant to F18 E. coli associated diseases**

  Inventor(s): Bosworth, Brad T.; (Littleton, NC), Vogeli, Peter; (Zurich, CH)

  Correspondence: Barnes & Thornburg; 2600 Chase Plaza; 10 Lasalle Street; Chicago; IL; 60603

  Patent Application Number: 20020129395

  Date filed: July 25, 2001

  Abstract: The present invention provides non-invasive methods and compositions to differentiate, with a high level of sensitivity and specificity, swine that are genetically susceptible to diseases associated with F18 E. coli infection, from resistant swine. DNA polymorphisms in the swine alpha (1,2) fucosyltransferase 1 (FUT1) gene were used to differentiate resistant from susceptible swine. The invention includes a polypeptide with amino acid substitutions, encoded by the nucleotide polymorphisms, a molecular diagnostic assay, and a kit for the differentiation, of E. coli F18-adhesion resistant, heterozygous (carrier) and homozygous susceptible pigs. The molecular test identifies susceptibility to oedema disease and postweaning **diarrhea** with high sensitivity and specificity, therefore, is useful to swine breeder in their effort to enhance for resistance. Information on the polymorphisms of the present invention provides insight into causation and treatment of E. coli associated intestinal disorders.

  Excerpt(s): This application claims priority to U.S. Provisional Application No. 60/047,181 filed May 10, 1997, now abandoned; PCT/US98/10318, filed May 20, 1998; and is a divisional of U.S. Ser. No. 09/443,766 filed Nov. 19, 1999. Compositions and non-invasive methods are provided for the identification of swine genetically resistant to E. coli bacteria supplied with fimbriae F18. DNA polymorphisms in the swine alpha (1,2) fucosyltransferase (FUT1) gene were identified that differentiate resistant from susceptible swine and provide a diagnostic test useful for swine breeders. A major problem in breeding swine is to keep them disease-free. Intestinal disorders postweaning are a particular problem. A limited number of serotypes of toxigenic Escherichia (E.) Coli strains are the causative agents of oedema disease and postweaning **diarrhea** in swine which induce serious economic losses, especially among piglets aged 4 to 2 weeks, in swine breeding farms all over the world. The typical symptoms of oedema disease are neurological signs such as ataxia, convulsions and paralysis. At post mortem examination, oedema is typically present at characteristic sites such as eyelids and forehead, stomach wall and mesocolon. The diseases are caused by Shiga-like toxin-II variant and enterotoxins LT, Sta, Stb respectively, produced by E. coli that colonize the surface of the small intestine without effecting major morphological changes of the enterocytes (cells in the intestine). Certain types of bacterial E. coli strains, F18, F4 and K88 are major lethal villains in this regard. "Oedema disease of pigs is an enterotoxaemia characterized by generalized vascular damage. The latter is caused by a toxin, Shiga-like toxin II variant, produced by certain strains of E. coli" (Bertschinger et al., 1993). The E. coli are distinguished by their pili types, a group of adhesive fimbriae that are related are designated e.g., K88 or F18 (Vogeli et al., 1997).

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

- **Compounds and method of treatment having agonist-like activity selective at alpha 2B or 2B / 2C adrenergic receptors**

  Inventor(s): Burke, James A.; (Santa Ana, CA), Chow, Ken; (Newport Coast, CA), Garst, Michael E.; (Newport Beach, CA), Gil, Daniel W.; (Corona Del Mar, CA), Harcourt, Dale A.; (San Clemente, CA), Munk, Stephen A.; (Northville, MI), Wheeler, Larry A.; (Irvine, CA)

  Correspondence: Allergan, INC.; T2-7h; Legal Department; 2525 Dupont Drive; Irvine; CA; 92612; US

  Patent Application Number: 20020156076

  Date filed: September 6, 2001

  Abstract: Compounds having adrenergic activity which are a selective agonists for one or both of the.alpha.sub.2B and.alpha.sub.2c adrenoceptor receptor subtypes in preference to the.alpha.sub.2A adrenoceptor receptor subtype; the active compound being selected from the group consisting of compounds having the formula 1wherein the dotted lines represent optional bonds provided that two double bonds may not share a common carbon atom; R is H or lower alkyl; X is S or C(H)R.sup.1, wherein R.sup.1 is H or lower alkyl, but R.sup.1 is absent when the bond between X and the ring represented by 2is a double bond; Y is O, N, S, (CR.sup.1.sub.2).sub.y, wherein y is an integer of from 1 to 3, --CH.dbd.CH-- or --Y.sup.1CH.sub.2--, wherein Y.sup.1 is O, N or S; x is an integer of 1 or 2, wherein x is 1 when R.sup.2, R.sup.3 or R.sup.4 is bound to an unsaturated carbon atom and x is 2 when R.sup.2, R.sup.3 or R.sup.4 is bonded to a saturated carbon atom; R.sup.2 is H, lower alkyl, halogen, hydroxy, lower alkoxy, lower alkenyl, acyl or lower alkynyl, or, when attached to a saturated carbon atom, R.sub.2 may be oxo; R.sub.3 and R.sub.4 are, each, H, lower alkyl, halogen, lower alkenyl, acyl, lower alkynyl, aryl, heteroaryl, or sub stituted aryl or heteroaryl, wherein said substituent is halogen, lower alkyl, lower alkoxy, lower alkenyl, acyl, lower alkynyl, nitro, cyano, trifluoromethyl, hydroxy, or phenyl or, together, are --(C(R.sup.2)x)z--; --Y.sup.1(C(R.sup.2)x)z'--; --Y.sup.1(C(R.sup.2)x)y Y.sup.1--; --(C(R.sup.2)x)--Y.sup.1--(C(R.sup.2)x)--; --(C(R.sup.2)x)--Y.sup.1--(C(R-.sup.2)x)--(C(R.sup.2)x)-- and --Y.sup.1--(C(R.sup.2)x)--Y.sup.1--(C(R.sup-.2)x)-- wherein z is an integer of from 3 to 5, z' is an integer of from 2 to 4 and x and y are as defined above, and further either end of each of these divalent moieties may attach at either R3 or R4 to form a condensed ring structure and the rings formed may be totally unsaturated, partially unsaturated, or totally saturated; and being useful for treating muscle spasticity including hyperactive micturition, **diarrhea,** diuresis, withdrawal syndromes, pain including neuropathic pain, neurodegenerative diseases, memory and cognition deficits, psychoses including manic disorders and anxiety, hypertension, cardiac ischemia, congestive heart failure, and nasal congestion without sedating or cardiovascular side effects.

  Excerpt(s): The present invention is directed to a method of treating glaucoma or elevated intraocular pressure and other diseases with substantially reduced cardiovascular or sedative side effects by administering to mammals including humans, compounds which are selective agonists of the.alpha.2B alone or.alpha.2B and.alpha.2C adrenergic receptor subtypes and which lack substantial activity at the.alpha.2A receptor subtype. The present invention is also directed to novel compounds and pharmaceutical compositions adapted for administering said compounds to mammals, including humans. Compounds which have adrenergic activity are well known in the art, and are described in numerous United States and foreign patents and in scientific publications. It is generally known and accepted in the art that adrenergic activity is useful for treating animals of the mammalian species, including humans, for curing or

alleviating the symptoms and conditions of numerous diseases and conditions. In other words, it is generally accepted in the art that pharmaceutical compositions having an adrenergic compound or compounds as the active ingredient are useful for treating glaucoma, chronic pain, nasal congestion, high blood pressure, congestive heart failure and inducing anesthesia. The two main families of adrenergic receptor are termed alpha adrenergic receptors and beta adrenergic receptors in the art, and each of these two families is known to have subtypes, which are designated by letters of the alphabet, such as.alpha.2A,.alpha.2B. See the article by Bylund et al, Pharmacol Rev. 46, pp. 121-136(1994).

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

- **Cyclic substituted aminomethyl compounds and medicaments comprising these compounds**

  Inventor(s): Koegel, Babette-Yvonne; (Langerwehe-Hamich, DE), Strassburger, Wolfgang Werner Alfred; (Wuerselen, DE), Zimmer, Oswald Karl; (Wuerselen, DE)

  Correspondence: Crowell & Moring Llp; Intellectual Property Group; P.O. Box 14300; Washington; DC; 20044-4300; US

  Patent Application Number: 20030166708

  Date filed: January 10, 2003

  Abstract: Cyclic substituted aminomethyl compounds of general formula IA and IB, methods for production thereof, intermediates in said production methods, a medicament containing at least one of said cyclic substituted aminomethyl compounds, the use of said cyclic substituted aminomethyl compounds for the production of a medicament, pharmaceutical compositions containing said compounds, and methods for the treatment of pain, incontinence, pruritis, tinnitus aurium and/or **diarrhea** using said pharmaceutical compositions.

  Excerpt(s): The present application is a continuation of international patent application no. PCT/EP01/07750, filed Jul. 6, 2001, designating the United States of America and published in German as WO 02/08218, the entire disclosure of which is incorporated herein by reference. Priority is claimed based on Federal Republic of Germany patent application no. 100 33 459.8, filed Jul. 10, 2000. The present Application relates to cyclic substituted aminomethyl compounds, processes for their preparation, intermediate compounds of these processes, medicaments comprising at least one of the cyclic substituted aminomethyl compounds, the use of the cyclic substituted aminomethyl compounds for the preparation of a medicament for treatment of pain, urinary incontinence, itching, tinnitus aurium and/or **diarrhea,** and pharmaceutical compositions comprising these compounds. Treatment of chronic and non-chronic states of pain is of great importance in medicine. There is a world-wide need for therapies which have a good action for target-orientated treatment of chronic and non-chronic states of pain appropriate for the patient, by which is to be understood successful and satisfactory pain treatment for the patient.

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

- **Detection of bovine viral diarrhea virus in hair samples**

  Inventor(s): Dubovi, Edward Joseph; (Ithaca, NY), Huchzermeier, Roy; (Fayetteville, NY)

  Correspondence: Michael L. Goldman; Nixon Peabody Llp; Clinton Square; P.O. Box 31051; Rochester; NY; 14603-1051; US

  Patent Application Number: 20030049610

  Date filed: August 9, 2002

  Abstract: The present invention relates to a method of detecting whether a target animal is Bovine Viral **Diarrhea** Virus (BVDV) positive or negative by determining whether a gp48 protein-specific reagent binds to a gp48 Bovine Viral **Diarrhea** Virus protein or protein fragment, which retains antigenic specificity, from a target animal's hair sample.

  Excerpt(s): This application claims the benefit of U.S. Provisional Patent Application Serial No. 60/311,212, filed on Aug. 9, 2001. The present invention relates to the detection of Bovine Viral **Diarrhea** Virus infection in hair samples from animals. Bovine viral **diarrhea** virus ("BVDV") currently represents a major threat to the cattle industry. First described over fifty years ago, this pathogen has been found to be both highly virulent and easily spread. Considered a primary pathogen of the bovine enteric, respiratory, reproductive, and immune systems, BVDV continues to cause significant economic losses to the cattle industry worldwide. Recent outbreaks have occurred in Canada, the United States, and throughout the world.

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

- **Effects of glucagon-like peptide-1 (7-36) on antro-pyloro-duodenal motility**

  Inventor(s): Goeke, Burkhard; (Gauting, DE), Schirra, Joerg; (Kirchhain, DE)

  Correspondence: Beth A. Burrous; Foley & Lardner; Washington Harbour; 3000 K Street, N.W., Suite 500; Washington; DC; 20007; US

  Patent Application Number: 20020098195

  Date filed: March 14, 2001

  Abstract: The present invention provides an effective method for inhibiting antro-duodenal motility in healthy subjects and patients suffering from various disorders, without the side effects associated with other pharmaceutical compositions. GLP-1 slows antro-duodenal motility and may be used for the treatment or prevention of gastrointestinal disorders such as **diarrhea,** postoperative dumping syndrome and irritable bowel syndrome, and also premedication in endoscopic procedures.

  Excerpt(s): The present invention relates to inhibiting antro-duodenal motility with GLP-1 and methods to alleviate discomfort during endoscopy and to alleviate symptoms of gastrointestinal disorders. Glucagon has been widely used to cause a variable reduction in gastroduodenal motility. The effect of glucagon appears to be dose-dependent with a minimally effective dose being 0.5 mg. Glucagon, however, does not facilitate colonoscopic evaluation (Norfleet, Gastrointest. Endosc., 24, 164-5, 1978), and at doses as high as 2 mg glucagon does not reduce contractions in the antrum (Gregerson et al., Scand. J. Gastroenterol. 23 (Supp 152), 42-47 (1988)). Furthermore, glucagon is contraindicated in persons with diabetes (Paul & Freyschmidt, ROFO Rortschr. Geb. Rontgenstr. Nuklearmed., 125, 31-7 (1996)), is expensive and its efficacy has been questioned. Side effects associated with the use of glucagon include nausea

and vomiting. The effects are dose-dependent and can appear at a dose of 1 mg (Larsen et al., Scand. J. Gastroenterol. 21, 634-640, 1986; Gregersen et al., supra, Diamant Handbook Experimental Pharm, Lefevre ed., Vol. 66/2, 611-643, 1983). As dosages required to sufficiently reduce motility frequently exceed 1 mg, side effects from glucagon use are common. Such side effects render the patient extremely uncomfortable and often cause the endoscopic procedure to be interrupted or aborted.

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

- **Enantiomerically pure opioid diarylmethylpiperzine and methods of using same**

  Inventor(s): Chang, Kwen-Jen; (Chapel Hill, NC)

  Correspondence: Intellectual Property / Technology Law; PO Box 14329; Research Triangle Park; NC; 27709; US

  Patent Application Number: 20030114462

  Date filed: September 25, 2002

  Abstract: (-)3-((S)-((2S,5R)-4-Allyl-2,5-dimethyl-1-piperazinyl)(3-thienyl)methyl)ph- enol and pharmaceutically acceptable esters or salts thereof, in essentially enantiomerically pure form have utility as receptor-binding species, e.g., as therapeutic agents for mediating analgesia; as co-administered agents with various other bioactive compositions, including anesthetics, barbiturates, analgesics, etc., for reducing, treating, reversing or preventing drug-mediated respiratory depression that may be directly or indirectly caused by use of such various bioactive compositions; as a conjugate in agonist/antagonist pairs for verifying/assaying receptor and neurotransmitter function; and as a therapeutic agent having utility in combating drug addiction, cardiac disorders, alcohol addiction, drug overdose, cough, lung edema, **diarrhea,** respiratory, and gastro-intestinal disorders.

  Excerpt(s): The present invention relates to a novel, essentially enantiomerically pure diarylmethylpiperazine compound having utility as a receptor-binding species, e.g., as a mu and/or delta receptor opioid compound mediating analgesia; as a therapeutic agent for co-administration with various other bioactive compositions, including anesthetics, barbiturates, analgesics, etc. for reducing, treating, reversing or preventing drug-mediated respiratory depression that may be directly or indirectly caused by use of such various bioactive compositions; as a conjugate in agonist/antagonist pairing for verifying/assaying receptor and neurotransmitter function; and as a therapeutic agent having utility in combating drug addiction, alcohol addiction, cardiac disorders, drug overdose, mental illness, cough, lung edema, **diarrhea,** respiratory, and gastro-intestinal disorders. In the study of opioid biochemistry, a variety of endogenous opioid compounds and non-endogenous opioid compounds has been identified. In this effort, significant research has been focused on understanding the mechanism of opioid drug action, particularly as it relates to cellular and differentiated tissue opiate receptors. Opioid drugs typically are classified by their binding selectivity in respect of the cellular and differentiated tissue receptors to which a specific drug species binds as a ligand. These receptors include mu (.mu.), delta (.delta.), sigma (.pi.) and kappa (.kappa.) receptors.

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

- **ESCHERICHIA COLI SECRETED PROTEIN B**

  Inventor(s): Jarvis, Karen; (Arnold, MD), Kaper, James B.; (Pasadena, MD)

  Correspondence: Andrea Doering; Tec Com/ord; University OF Maryland, Baltimore; 515 West Lombard Street, Suite 500; Baltimore; MD; 21201-1602; US

  Patent Application Number: 20030166841

  Date filed: January 24, 2001

  Abstract: Several EHEC proteins which are secreted into the culture supernatant have been discovered. These proteins are not produced by non-pathogenic E. coli, and produce a strong serum antibody response in patients with HUS and bloody **diarrhea.**

  Excerpt(s): The present invention relates to novel proteins which are secreted from enterohemorrhagic Escherichia coli (EHEC), a pathogen responsible for bloody **diarrhea** and hemolytic uremic syndrome (HUS) in humans. The invention relates to serodiagnostic techniques of these conditions using these proteins. The most common cause of bloody **diarrhea** and hemolytic uremic syndrome (HUS) in North America is infection by enterohemorrhagic E. coli (EHEC) (1). Alternative names for EHEC are Shiga toxin-producing E. coli (STEC), Shiga-like toxin-producing E. coli (SLTEC), Verocytotoxin-producing E. coli (VTEC), or Verotoxin-producing E. coli. In the United States, this food-borne E. coli is the most common infectious cause of bloody **diarrhea** in individuals of all ages. HUS is the most common cause of kidney failure in children in the U.S. and Canada. This organism was the cause of the infamous "Jack-in-the-Box" food-poisoning outbreak in Seattle in 1993 which infected over 500 people and resulted in 4 deaths and many cases of long-term kidney damage. In 1996, this organism caused an enormous outbreak involving more than 8,000 people in Japan, resulting in 7 deaths. In late 1996, EHEC again caused an outbreak of food-poisoning in Scotland which affected 250 people and killed 18 people.

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

- **Generation of type I/type II hybrid form of bovine viral diarrhea virus for use as vaccine**

  Inventor(s): Cao, Xuemei; (East Lyme, CT), Zybarth, Gabriele M.; (Little Compton, RI)

  Correspondence: Peter I. Bernstein; Scully, Scott, Murphy & Presser; 400 Garden City Plaza; Garden City; NY; 11530; US

  Patent Application Number: 20030104612

  Date filed: August 27, 2002

  Abstract: The present invention provides genetically engineered type I/type II hybrid BVDV viruses. The hybrid viruses, as well as the hybrid viral genome, can be used in immunogenic compositions and vaccines for protecting cattle from BVDV infection.

  Excerpt(s): This application claims the benefit of U.S. Provisional Patent Application No. 60/315,445 filed Aug. 28, 2001, the contents of which are hereby incorporated by reference in its entirety. The present invention relates to genetically engineered type I/type II hybrid BVDV viruses. The hybrid viruses, as well as the hybrid viral genome, can be used in vaccines for protecting cattle from BVDV infection. Bovine viral **diarrhea** (BVD) virus is classified in the pestivirus genus and Flaviviridae family. It is closely related to viruses causing border disease in sheep and classical swine fever. Infected cattle exhibit "mucosal disease" which is characterized by elevated temperature,

diarrhea, coughing and ulcerations of the alimentary mucosa (Olafson, et al., Cornell Vet. 36:205-213 (1946); Ramsey, et al., North Am. Vet. 34:629-633 (1953)). The BVD virus is capable of crossing the placenta of pregnant cattle and may result in the birth of persistently infected (PI) calves (Malmquist, J. Am. Vet.Med. Assoc. 152:763-768 (1968); Ross, et al., J. Am. Vet Med. Assoc. 188:618-619 (1986)). These calves are immunotolerant to the virus and persistently viremic for the rest of their lives. They provide a source for outbreaks of mucosal disease (Liess, et al., Dtsch. Tieraerztl. Wschr. 81:481-487 (1974)) and are highly predisposed to infection with microorganisms causing diseases such as pneumonia or enteric disease (Barber, et al., Vet. Rec. 117:459-464 (1985)).

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

- **Isolation, characterization, cloning and use of a mushroom lectin**

  Inventor(s): Goldstein, Irwin J.; (Ann Arbor, MI), Kruger, Robert P.; (Ann Arbor, MI), Winter, Harry C.; (Ann Arbor, MI)

  Correspondence: Medlen & Carroll, Llp; Suite 350; 101 Howard Street; San Francisco; CA; 94105; US

  Patent Application Number: 20030092109

  Date filed: May 2, 2002

  Abstract: The isolation, characterization, cloning and expression of the lectin (agglutinin) from Marasmius oreades (MOA) is described. MOA displays unique carbohydrate binding properties, including blood group B-specific agglutination and preferential binding to Gal.alpha.1,3Gal-containing sugar epitopes, including but not limited to Gal.alpha.1,3Gal.beta.1,4Glc- NAc. MOA is contemplated as an affinity reagent, a therapeutic in the treatment of antibiotic-induced **diarrhea** and the field of xenotransplantation. MOA may also serve as a diagnostic reagent, e.g. for malaria.

  Excerpt(s): This application claims the benefit of U.S. Provisional Application Serial No. 60/288,596, filed on May 3, 2001 and U.S. Provisional Application Serial No. 60/354,322, filed on Feb. 4, 2002. The invention relates to the field of carbohydrate binding proteins, and more specifically a protein which binds specifically to particular oligosaccharides associated with particular medical significance. The Gal.alpha.1,3Gal epitope has received considerable attention stemming from its presence in glycoproteins of most mammals and its conspicuous absence in humans, apes, and Old World monkeys. The loss is attributable to frameshift mutations in.alpha.,3-galactosyltransferase and the resulting immunogenicity of the epitope is a significant barrier to xenotransplantation.

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

- **Materials and methods for the treatment of gastroesophageal reflux disease**

  Inventor(s): Becker, Cyrus; (Menlo Park, CA), Druzgala, Pascal; (Santa Rosa, CA), Milner, Peter G.; (Los Altos Hills, CA), Pfister, Jurg; (Los Altos, CA)

  Correspondence: Saliwanchik Lloyd & Saliwanchik; A Professional Association; 2421 N.W. 41st Street; Suite A-1; Gainesville; FL; 326066669

  Patent Application Number: 20030216387

  Date filed: April 18, 2003

Abstract: The subject invention provides novel compounds and compositions for the safe and effective treatment of gastroesophageal reflux and related conditions. In a preferred embodiment, the compositions of the subject invention comprise esterified cisapride derivatives. These compositions possess potent activity in treating gastroesophageal reflux disease and substantially reduce adverse effects associated with the administration of cisapride. These adverse effects include, but are not limited to, **diarrhea,** abdominal cramping and elevations of blood pressure and heart rate.

Excerpt(s): This application is a continuation of co-pending application Ser. No. 09/876,698, filed Jun. 7, 2001 (pending). The subject application also claims priority to provisional application U.S. Serial No. 60/209,926, filed Jun. 7, 2000. Cisapride is one of a class of compounds known as benzamide derivatives, the parent compound of which is metoclopramide. U.S. Pat. Nos. 4,962,115 and 5,057,525 (collectively "Van Daele" and incorporated by reference in their entireties) disclose N-(3-hydroxy-4-piperidenyl) benzamides of cisapride. Van Daele discloses that these compounds, the pharmaceutically acceptable acid addition salts thereof and the stereochemically isomeric forms thereof, stimulate the motility of the gastrointestinal system. As a class, these benzamide derivatives have several prominent pharmacological actions. The prominent pharmacological activities of the benzamide derivatives are due to their effects on the neuronal systems which are modulated by the neurotransmitter serotonin. The role of serotonin, and thus the pharmacology of the benzamide derivatives, has been broadly implicated in a variety of conditions for many years. Thus, research has focused on locating the production and storage sites of serotonin as well as the location of serotonin receptors in the human body in order to determine the connection between these sites and various disease states or conditions.

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

- **Medicinal compositions promoting bowel movement**

Inventor(s): Asano, Osamu; (Ibaraki, JP), Harada, Hitoshi; (Ibaraki, JP), Harada, Kokichi; (Ibaraki, JP), Hida, Takayuki; (Ibaraki, JP), Kobayashi, Seiichi; (Belmont, MA), Kotake, Yoshihiko; (Ibaraki, JP), Miyazawa, Shuhei; (Ibaraki, JP), Shibata, Hisashi; (Ibaraki, JP), Yasuda, Masahiro; (Ibaraki, JP), Yasuda, Nobuyuki; (Ibaraki, JP)

Correspondence: Birch Stewart Kolasch & Birch; PO Box 747; Falls Church; VA; 22040-0747; US

Patent Application Number: 20030171383

Date filed: October 9, 2002

Abstract: The present invention provides a medicament having a gentle but strong defecation-promoting action without causing **diarrhea.** That is, it provides a defecation-promoting agent comprising a compound having an adenosine A.sub.2 receptor antagonism, preferably an adenosine A.sub.2b receptor antagonism, or a salt thereof.

Excerpt(s): The present invention relates to a novel pharmaceutical composition promoting defecation, and to a novel pyrimidine compound or a salt thereof. Constipation refers to a condition where defecation is difficult or rare, and this is a well-known disease. Known constipation is divided mainly into e.g. functional constipation (acute constipation and various kinds of chronic constipation (for example, atonic constipation, spastic constipation, dyschezia, rectal constipation, chemically inducible constipation etc.)), organic constipation, enteroparalytic ileus, IBS, constipation accompanying IBS, constipation accompanying congenital digestive tract dysfunction,

constipation accompanying ileus etc. In defecation in the normal state, stimulation of rectal mucous with intestinal contents transferred to the rectum is transmitted to the central nerve, thus inducing an inclination for the stool while causing the bowels and muscles to be reflectively relaxed and contracted (defecating reflex), while constipation occurs due to defecating functions ruined by autonomic nervous dysfunction occurred in digestive tracts, hyper-absorption of water into intestinal tracts, a reduction in secretion of intestinal mucus, motility hindrance, digestive psychosomatic disease in the digestive organs (for example, irritable bowel syndrome (IBS), a reduction in defecating reflective functions, etc. Many of these obstacles are caused by eating habits, life-style, physical activity, psychogenic background (mental stress, emotional instability, etc.). Recently, such constipation is a serious problem in the fields of nursing and clinical and medical cure. As one of factors, there is a rapid increasing number of old people in the society in recent years and an increase in old peoples requiring nursing. Patients with constipation (for example, atonic constipation) attributable to autonomous nervous dysfunction are rapidly increasing. Another factor is an increase in diseases readily causing a reduction in the motility function of digestive tracts. In particular, diabetes is one of serious diseases, and is problematic as complications to cause a rapid increase in patients with constipation. This is called symptomatic constipation, and also observed in hypothyroidism, sclerodermia, cerebrovascular disturbances, depression, spinal disturbances, electrolyte abnormalities, uremia, interstitial lung disease, pulmonary emphysema and various nerve diseases. In addition to these, there are really many reports on patients with spastic constipation accompanying IBS observed often in youths, on patients with chemically inducible constipation induced by use of morphine in cancer patients, etc. Prescriptions such as a laxative and an enema are conventionally used in principal therapeutic methods. However, these chemicals easily cause **diarrhea** upon administration thereof, give physical and mental suffering to the patients and nurses, and usually require a long time until their action appears, and their action is long-lasting. There is also a problem that overuse of an enema also causes disappearance of an inclination for the stool. Further, when the patient has high blood pressure or may have cerebral apoplexy, cerebral infarction, cardiac infarction etc., there is also the situation where an enema should be used inevitably to prevent such diseases. Accordingly, if there is a medicine gently promoting defecation without generating **diarrhea,** the medicine can be expected to be very useful and advantageous to many patients and nurses, and there is demand for providing the medicament. However, a medicine satisfactory in these aspects is still not found.

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

- **Method and composition for the treatment of diarrhea and gastrointestinal spasms**

  Inventor(s): Bergeron, Raymond J.; (Gainesville, FL)

  Correspondence: Miles & Stockbridge; 1751 Pinnacle Drive, Suite 500; Mclean; VA; 22102-3833; US

  Patent Application Number: 20020193408

  Date filed: March 7, 2002

  Abstract: Anti-diarrheal and/or gastrointestinal anti-spasmodic pharmaceutical compositions containing [A] a polyamine of the formula:R.sub.1--N.sup.1(R.sub.2)--(CH.sub.2)x-N.sup.2H--Q--N.sup.3H--(CH.sub.2)y-- N.sup.4(R.sub.3)--R.sub.4 (I)wherein: R.sub.1, R.sub.2, R.sub.3 and R.sub.4 may be the same or different and are H, alkyl, cycloalkyl or aralkyl having from 1 to 12 carbon atoms, or a heterocyclic group

having from 3 to 10 atoms wherein the hetero atom is said N.sup.1 or N.sup.4;Q is a cycloalkyl group having from 3 to 10 carbon atoms;x is an integer from 3 to 6, inclusive;and y is an integer from 3 to 6, inclusive;or (II) a salt thereof with a pharmaceutically acceptable acid; and [B] a pharmaceutically acceptable carrier therefor as well as methods of treatment utilizing the polyamines are disclosed.

Excerpt(s): The present invention relates to certain novel anti-diarrheal and gastrointestinal anti-spasmodic agents and methods of treatment and pharmaceutical compositions based thereon. Diarrhea can result from a variety of pathophysiological disorders including bacterial and parasitic infections, disease or debilitation of organs such as liver, adrenal and others. It can also occur as a result of other therapy or diet. In all cases, **diarrhea** is generally a symptom of organic gastrointestinal disorders and not itself a disorder. Chronic **diarrhea** is generally due to: (1) hypersecretion of fluid and electrolytes of the stomach, small intestine and colon; (2) inability to absorb certain nutrients (malabsorption); and (3) intestinal hypermotility and rapid transport. These may occur separately or in combination. Certain disorders may have **diarrhea** as a prominent feature of the disease/syndrome, but the specific etiology is unclear. In this latter group, emotional tension and psychological factors may adversely influence the frequency of the symptoms. Diarrhea and diarrheal diseases are one of the most frequent causes of morbidity and mortality, especially in less developed countries wherein the number of those killed by such diseases is estimated at about 5 million persons per annum. Particularly dangerous are diarrheal diseases of the newborn and the youngest group of babies (S. Hughes: Drugs, Vol. 26, pp. 80-90 (1983)).

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

- **Method for management of blood glucose levels**

  Inventor(s): Heyliger, Clayton; (Manitoba, CA), Pierce, Grant; (Manitoba, CA)

  Correspondence: Ade & Company; 1700-360 Main Street; Winnipeg; MB; R3c3z3; CA

  Patent Application Number: 20030108625

  Date filed: September 17, 2002

  Abstract: A composition for managing blood glucose levels is herein described. The composition comprises decocted tea and vanadate and does not cause the same side effects as vanadate and water mixtures known in the prior art. Specifically, the vanadate suspended in decocted tea does not cause **diarrhea** and in some cases stabilizes blood glucose at normal levels for several weeks after only a few treatments.

  Excerpt(s): This application is derived from Provisional Patent Application Serial No. 60/135,653 filed on May 24, 1999 and is a continuation-in-part of U.S. Ser. No. 09/576,130, filed May 22, 2000. The present invention relates generally to a pharmaceutical composition. More specifically, the present invention relates to a pharmaceutical composition for managing blood glucose levels. Since the discovery of insulin by Banting and Best, regular insulin injections have remained the best and most frequently used therapy to control abnormal blood glucose levels in diabetic patients (Pierce et al in Heart Dysfunction in Diabetes (CRC Press: Boca Raton, Fla., 1988). The use of insulin has significantly prolonged the life of diabetic patients and reduced the severity of many complications associated with this disease. Besides insulin, only the sulfonylurea drugs have gained widespread use for the control of diabetes (Pierce et al, 1988).

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

- **Method for reducing chloride secretion by intestinal epithelial cells in situ: use of triaryl methane compounds**

  Inventor(s): Alper, Seth; (Jamaica Plains, MA), Brugnara, Carlo; (Newton Highlands, MA), Lencer, Wayne I.; (Jamaica Plains, MA)

  Correspondence: Chantal Morgan D'apuzzo; Wolf, Greenfield & Sacks, P.C.; 600 Atlantic Avenue; Boston; MA; 02210; US

  Patent Application Number: 20030119784

  Date filed: November 8, 2002

  Abstract: A method and product for treating and preventing **diarrhea** and scours is provided. The method involves treating a subject who has **diarrhea,** or scours, or is at risk of getting **diarrhea** or scours with an aromatic compound of the invention. The products of the invention are a veterinary preparation of the aromatic compound of the invention and an anti-scours agent, and a pharmaceutical preparation of the aromatic compound of the invention and an anti-diarrheal agent.

  Excerpt(s): This application is a continuation-in-part of application Ser. No. 08/621,169, filed Mar. 20, 1996, now pending, which is incorporated herein in its entirety by reference. The present invention relates to methods and products for reducing chloride secretion using aromatic organic compounds. In particular the invention relates to methods of treating **diarrhea** and scours by administering triaryl methane compounds. Acute and chronic diarrheas represent a major medical problem in many areas of the world. **Diarrhea** is both a significant factor in malnutrition and the leading cause of death (5,000,000 deaths/year) in children less than five years old. Secretory diarrheas are also a dangerous condition in patients of acquired immunodeficiency syndrome (AIDS) and chronic inflammatory bowel disease (IBD). 16 million travelers to developing countries from industrialized nations every year develop **diarrhea,** with the severity and number of cases of **diarrhea** varying depending on the country and area of travel. The major medical consequences of diarrheal diseases include dehydration, acidosis, death and impaired growth.

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

- **Method for the production of the egg containing anti-pathogenic bacteria specific antbodies(igy) and the yogurt and ice cream containing the igy**

  Inventor(s): Baek, Ban-Suk; (Gyeonggi-do, KR), Jung, Kwnag-Yong; (Daejeon, KR), Lee, Nam-Hyung; (Seoul, KR), Ryu, Jung-Soo; (Daejeon, KR), Sunwoo, Sun-Young; (Seoul, KR)

  Correspondence: Fleshner & Kim; PO Box 221200; Chantilly; VA; 20153-1200; US

  Patent Application Number: 20030185856

  Date filed: November 27, 2002

  Abstract: The present invention provides the method for the production of the egg containing anti-pathogenic bacteria specific antibodies (IgY) preventing gastritis, **diarrhea,** and food poisoning by immunizing young hens with antigen proteins of E. coli causing enteritis, Helicobacter pylori causing gastritis, and Salmonella enteritidis and Salmonella typhimurium, causing food poisoning, simultaneously. This invention also relates to composition containing the specific IgY antibodies described above and

the foodstuff such as the yogurt and ice cream containing the anti-pathogenic IgY.Additionally, the present invention provides the separation method of the IgY containing protein powders from egg yolk. particularly, this separation method involves diluting egg yolk with water at 1:1 ratio and adding the appropriate amount of ammonium sulfate which enables water-soluble protein and phospholipid to separate.

Excerpt(s): Additionally, as the method for isolating the protein powders of the specific antibodies, the method for separating protein and phospholipid, particularly, proceeded in a process of diluting egg yolk with distilled water in 1:1 ratio, adding the appropriate amount of ammonium sulfate which enable water-soluble protein and phospholipid to separate, and the method for separating the pigment of egg-yolk and water-soluble protein, proceeded in a process of diluting those separated solution with distilled water, sitting in the certain temperature to precipitate and purify the proteins. The prior art related to patent of E.1coli is summarized as following.

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

- **Methods of administering camptothecin compounds for the treatment of cancer with reduced side effects**

Inventor(s): Bouscarel, Bernard; (Arlington, VA), Kobayashi, K.; (Urawa-City, JP)

Correspondence: Antonelli Terry Stout And Kraus; Suite 1800; 1300 North Seventeenth Street; Arlington; VA; 22209

Patent Application Number: 20020193391

Date filed: June 17, 2002

Abstract: Methods of administering camptothecin compounds such as irinotecan hydrochloride to reduce a **diarrhea** side effect and methods of treating cancer and AIDs with camptothecin compounds including administering the camptothecin compounds while maintaining the intestinal lumen and the bile at an alkaline pH.

Excerpt(s): The present invention relates to camptothecin compounds, in particular, irinotecan hydrochloride composition formulations, and methods of administering camptothecin compounds such as irinotecan hydrochloride for the treatment of cancer and AIDS, with reduced side effects. Camptothecin is a quinoline-based alkaloid found in the barks of the Chinese Camptotheca tree and the Asian nothapodytes tree. It is a close chemical relative to aminocamptothecin, CPT-11 (irinotecan), DX-8951F and topotecan. These compounds are useful in treating breast cancers, ovarian cancer, colon cancer, malignant melanoma, small cell lung cancer, thyroid cancers, lymphomas and leukemias. These compounds are also used for the treatment of AIDS. Irinotecan hydrochloride (CPT-11) (4S)-4,11-diethyl-4-hydroxy-9-[(4- -piperidinopiperidino)carbonyloxy]1H-pyrano [3', 4':6,7] indolizino,[1,2-b]quinoline-3,14(4 h,12H)dione hydrochloride, has a novel mechanism of antitumor activity, namely the inhibition of DNA topoisomerase I. Topoisomer-ases are the enzymes which wind and unwind the DNA that makes up the chromosomes. As the chromosomes must be unwound to make proteins, camptothecin compounds keep the chromosomes wound tight so that they cannot make proteins. Because cancer cells grow at a much faster rate than normal cells, they are more vulnerable to topoisomerase inhibition than normal cells.

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

- **Pestivirus mutants and vaccines containing the same**

  Inventor(s): Becher, Paul P.; (Fronhausen, DE), Orlich, Michaela M.; (Giessen, DE), Thiel, Heinz-Jurgen H.J.; (Giessen, DE)

  Correspondence: William M. Blackstone; Akzo Nobel; 1300 Piccard Drive #206; Rockville; MD; 20850-4373; US

  Patent Application Number: 20020086033

  Date filed: April 19, 2001

  Abstract: The present invention is directed to attenuated pestivirus mutants, which have a reduced ability to replicate as exhibited by a small plaque size. The mutations are in the 5' nontranslated region of the viral genome. These mutant viruses are useful as live vaccines in the control of bovine viral **diarrhea,** border disease and classical swine fever.

  Excerpt(s): The present invention is directed to attenuated pestivirus mutants, which have a reduced ability to replicate, which is exhibited by a small plaque size. Such viruses are useful as live vaccines in the control of bovine viral **diarrhea,** classical swine fever and border disease of sheep. The invention is particularly directed to attenuated bovine viral **diarrhea** viruses that have been genetically engineered for reduced replication in the host, and which are useful in live vaccines for cattle. Pestiviruses cause economically important diseases in animals worldwide. The genus Pestivirus, within the family Flaviviridae, comprises three species: bovine viral **diarrhea** virus (BVDV), classical swine fever virus (CSFV), and border disease virus (BDV). The presence of a fourth separate group of pestiviruses comprising isolates from cattle and sheep has been recently described, and it is now generally accepted to refer to this additional species as BVDV-2; consequently, classical BVDV strains are named BVDV-1. See Becher et al., Virology 209(1):200-206 (1995). BVDV-1 and BVDV-2 both cause acute infections in cattle (diarrhea, fever, hemorrhagic syndrome) as well as (if the infection occurs during pregnancy) abortion, malformation of the fetus and persistent infection of the calves. Persistently infected animals represent the major reservoir of the virus, and such animals may come down with the fatal mucosal disease (MD).

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

- **Polynucleotide vaccine formula in particular against bovine respiratory pathology**

  Inventor(s): Audonnet, Jean-Christophe; (Lyon, FR), Baudu, Philippe; (Craponne, FR), Bouchardon, Annabelle; (Lyon, FR), Riviere, Michel; (Ecully, FR)

  Correspondence: Frommer Lawrence & Haug; 745 Fifth Avenue- 10th FL.; New York; NY; 10151; US

  Patent Application Number: 20020160018

  Date filed: February 28, 2002

  Abstract: Disclosed and claimed are compositions for inducing in a bovine host an immunological response against bovine respiratory syncytial virus or bovine viral **diarrhea** virus containing at least one plasmid that contains and expresses in vivo in a bovine host cell nucleic acid molecule(s) having sequence(s) encoding bovine respiratory syncytial virus F protein, or G protein, or F and G proteins; or, at least one plasmid that contains and expresses in vivo in a bovine host cell nucleic acid molecule(s) having sequence(s) encoding bovine viral **diarrhea** virus E2 protein, or C, E1 and E2

proteins, or E1 and E2 proteins. Methods and kits employing such compositions are also disclosed.

Excerpt(s): The present invention relates to a vaccine formula allowing the vaccination of bovines in particular against respiratory pathology. It also relates to a corresponding method of vaccination. All bovines are carriers of viruses and bacteria which are potentially pathogenic in widely variable degrees. Viruses can multiply when the specific immunity is weakened and when there are lesions of the respiratory tract. They are then excreted by the animal and may then contaminate other animals.

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

- **Predicting patient responsiveness to serotonergic therapy**

  Inventor(s): Camilleri, Michael L.; (Rochester, MN), Urrutia, Raul A.; (Rochester, MN)

  Correspondence: Fish & Richardson P.C.; 3300 Dain Rauscher Plaza; 60 South Sixth Street; Minneapolis; MN; 55402; US

  Patent Application Number: 20030143548

  Date filed: January 28, 2002

  Abstract: Methods to predict a patient's responsiveness to 5-HT.sub.3 receptor antagonists are disclosed. The methods allow a clinician to predict a patient's responsiveness to 5-HT.sub.3 receptor antagonists by determining the correlation that exists between a genotype in the promoter region of the gene encoding a serotonin transporter protein and patient response to 5-HT.sub.3 receptor antagonist therapy. In addition, methods to treat patients suffering from diarrhea-predominant irritable bowel syndrome and methods to identify a patient population for inclusion in a 5-HT.sub.3 receptor antagonist clinical trial are disclosed.

  Excerpt(s): Funding for the work described herein was provided in part by the Federal Government, which may have certain rights in the invention. This invention relates to serotonergic therapy, and more particularly to predicting a patient's responsiveness to serotonergic receptor antagonists. Irritable bowel syndrome (IBS) is a common gastrointestinal disorder in western populations, with an adult prevalence of approximately 15%. The cardinal features of IBS are recurrent abdominal pain and altered bowel habits. Diarrhea-predominant IBS has been associated with accelerated small bowel and/or colonic transit and with rectal hypersensitivity.

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

- **Preparation for preventing bile acid diarrhea**

  Inventor(s): Hayakawa, Hiroshi; (Settsu-shi, JP), Masuda, Kazuyoshi; (Osaka-shi, JP), Sugita, Katsuji; (Osaka-shi, JP), Suzuki, Yusuke; (Settsu-shi, JP), Syodai, Hidekazu; (Amagsaki-shi, JP)

  Correspondence: Wenderoth, Lind & Ponack, L.L.P.; 2033 K Street N. W.; Suite 800; Washington; DC; 20006-1021; US

  Patent Application Number: 20030124088

  Date filed: October 8, 2002

Abstract: Preparations for preventing bile acid **diarrhea** which comprise containing a bile acid adsorbent coated with a polymer so as to allow the release thereof around an area from the lower part of the small intestine to the cecum; and pharmaceutical compositions comprising a combination of bile acid re-absorption inhibitors with the above preparations for preventing bile acid **diarrhea** (e.g., antihyperlipidaemic agent).

Excerpt(s): The present invention relates to a preparation for preventing bile acid **diarrhea,** a pharmaceutical composition which comprises a combination of a bile acid re-absorption inhibitor and the preparation for preventing **diarrhea,** and the like. It was reported by LRC-CPPT (Lipid Research Clinics Coronary Primary Prevention Trial), U.S.A, in 1984 that the crisis rate of coronary artery disease can be reduced by the treatment of hypercholesterolemia using a bile acid excretion-accelerating agent. Since then, various hypercholesterolemia-treating agents based on the pharmacological mechanism have been developed. Among them, bile acid re-absorption inhibitors, such as lignan analogs (JP Patent Publication (A) 1993/310634, U.S. Pat. No. 5,420,333) or glucuronic acid conjugates thereof (JP Patent Publication (A) 1997/241206) etc.), are known to inhibit the re-absorption of bile acid from the small intest by the inhibition of bile acid transporter (BAT), so as to lower the concentration of LDL-cholesterol. However, the inhibition of the re-absorption of bile acid leads to a large quantity of flow of the bile acid into the large intestine, causing the increase of the bile acid concentration therein. In such a case, there is a concern that bile acid **diarrhea** may be induced in the large intestine depending on the type of patients, health status thereof, or the like. On the contrary, bile acid adsorbents, such as anion-exchange resins represented by cholestyramine, are known to inhibit the enterohepatic circulation of bile acid by absorbing bile acid in the intestinal tract to excrete it into excrement, whereby to lower the LDL-cholesterol concentration. For example, JP Patent Publication (A) 1988/152321 discloses a preparation of cholestyramine for sustained-release inside gastrointestinal, wherein the surface thereof is coated so as to stabilize the preparation until it reaches the top of the small intestine for the purpose of maximizing the efficacy of cholestyramine.

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

- **Prevention and treatment of digestive tract infections**

Inventor(s): Franklin, Lanny Udell; (Atlanta, GA), Pimentel, Julio L.; (Buford, GA)

Correspondence: Julio L. Pimentel, PH.D.; 3206 Windgate DR.; Buford; GA; 30519-1941; US

Patent Application Number: 20030157159

Date filed: January 15, 2002

Abstract: Prevention and treatment of digestive tract infections in humans and animals by orally administering a single terpene, a terpene mixture or a liposome-terpene(s) composition before or after the onset of a gastro-intestinal infection. Such infections may include traveler's **diarrhea,** ulcers, anthrax and other bacterial and parasitical infections.

Excerpt(s): Prevention and treatment of digestive tract infections in humans and animals by orally administering a single terpene, a terpene mixture or a liposome-terpene(s) composition before or after the onset of the infection, single terpenes having biocidal activity which in combination with two or more other terpenes synergistically increase the biocidal effectiveness. Digestive tract infections are mainly caused by pathogenic and opportunistic microorganisms and toxins produced by them. These illnesses are present in all types of animals and humans. Recently with the scare of bio-terrorism

there has been an increased concern with pathogens that can produce deadly outbreaks. This is the case with anthrax. Anthrax is considered a potential agent for use in biological warfare. Anthrax is an acute infectious disease caused by the spore-forming bacteria Bacillus anthracis. Anthrax is primarily a disease of domesticated and wild animals, particularly herbivorous animals. Humans become infected with anthrax by handling products from infected animals or by inhaling anthrax spores from contaminated animal products. Anthrax can also be spread by eating undercooked meat from infected animals. Anthrax infection can occur in three forms: cutaneous, inhalation, and gastrointestinal. The most common form is the cutaneous anthrax infection, which occurs when bacteria enter a cut or abrasion on the skin. This infection begins as a raised itchy bump that develops into a vesicle and then a painless ulcer, usually 1-3 cm in diameter, with a characteristic black necrotic area in the center. About 20% of untreated cases of cutaneous anthrax result in death. Deaths may be prevented with prompt antimicrobial treatment. The inhalation form has early symptom similar to a common cold which progressively results in severe breathing problems. This type of anthrax is usually fatal. The intestinal form is characterized by an acute inflammation of the intestinal tract. The initial signs are nausea, loss of appetite, vomiting, and fever followed by abdominal pain, vomiting of blood and severe **diarrhea.** Intestinal anthrax results in death in 25% to 60% of cases. Anthrax is treated with antimicrobials and can be prevented with vaccination. The Department of Defense in the USA has a mandatory anthrax vaccination of all active military personnel.

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

- **Selective antagonists of A2B adenosine receptors**

  Inventor(s): Biaggioni, Italo O.; (Nashville, TN), Feoktistov, Igor A.; (Nashville, TN), Wells, Jack N.; (Nashville, TN)

  Correspondence: A. Blair Hughes; Mcdonnell Boehnen Hulbert & Berghoff; 32nd Floor; 300 S. Wacker Drive; Chicago; IL; 60606; US

  Patent Application Number: 20030087904

  Date filed: November 1, 2002

  Abstract: A compound of the following formula: 1wherein R is an aliphatic or cycloaliphatic amine group or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable salt thereof. The compounds of formula (I) may be used to treat, among other indications, asthma and **diarrhea.**

  Excerpt(s): The present invention relates to novel pharmaceutical compounds useful as selective antagonists of the A.sub.2B adenosine receptor. Furthermore, the present invention relates to novel pharmaceutical compositions useful for treating certain indications including asthma and **diarrhea.** The present invention also relates to novel methods of treating certain indications including asthma and **diarrhea.** There is substantial evidence that adenosine modulates many physiological processes. Its actions are mediated by interaction with specific cell membrane receptors. Four types of adenosine receptors have been identified: A.sub.1, A.sub.2A, A.sub.2B and A.sub.3. All four subtypes have been cloned from human tissue. Adenosine receptors have the seven transmembrane domain structure typical of G protein-coupled receptors. Adenosine receptors are widely distributed throughout the body and are probably present in every cell. Adenosine receptors were initially classified by the ability to inhibit (A.sub.1) or activate (A.sub.2 and A.sub.2B) adenylate cyclase. A.sub.3 receptors also inhibit adenylate cyclase. Modulation of adenylate cyclase is mediated through coupling to

G.sub.s and G.sub.i guanine-nucleotide regulatory proteins. It is now known that adenosine receptors are also coupled to other intracellular signaling pathways. A.sub.1 and A.sub.3 receptors, for example, can couple to phospholipase C; A.sub.1 receptors are also coupled to K channels. A.sub.2B receptors are also coupled to Gq and mediate activation of PLC, Ras and MAP kinases.

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

- **Substituted 3,4-dihydro-pyrimido[1,2a]pyrimidines and 3,4-dihydro-pyrazino[1,2a]pyrimidines, and methods for their preparation and use**

  Inventor(s): Gerlach, Matthias; (Brachttal, DE), Jagusch, Utz-Peter; (Aachen, DE), Maul, Corinna; (Aachen, DE)

  Correspondence: Crowell & Moring Llp; Intellectual Property Group; P.O. Box 14300; Washington; DC; 20044-4300; US

  Patent Application Number: 20030220322

  Date filed: April 9, 2003

  Abstract: Substituted 3,4-dihydro-pyrimido[1,2a]pyrimidines and 3,4-dihydro-pyrazino[1,2a]pyrimidines of general formula I, the invention also relates to a method for the production thereof, substance libraries containing these compounds, medicaments which contain these compounds in the production of medicaments for treating pain, urinary incontinence, itching, tinnitus aurium and/or **diarrhea** and to pharmaceutical compositions containing these compounds.

  Excerpt(s): The present application is a continuation of International Patent Application No. PCT/EP01/11702, filed Oct. 10, 2001, designating the United States of America and published in German as WO 02/30934 A1, the entire disclosure of which is incorporated herein by reference. Priority is claimed based on Federal Republic of Germany Patent Application No. 100 50 661.5, filed Oct. 13, 2000. The present application relates to substituted 3,4-dihydro-pyrimido[1,2a]pyrimidines and 3,4-dihydro-pyrazino[1,2a]pyrim- idines, to methods for their production, to substance libraries containing them, to pharmaceutical preparations which contain these compounds, to the use of these compounds for producing pharmaceutical preparations to treat pain, urinary incontinence, itching, tinnitus aurium and/or **diarrhea** and to pharmaceutical compositions containing these compounds. The treatment of chronic and non-chronic pain conditions has great importance in medicine. There is a worldwide need for effective therapies for patient-friendly and targeted treatment of chronic and non-chronic pain conditions, especially the successful and satisfactory treatment of pain for the patient.

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

- **Use of isatin derivatives as ion channel activating agents**

  Inventor(s): Ahring, Philip K.; (Bagsvard, DK), Christophersen, Palle; (Ballerup, DK), Jensen, Bo Skaaning; (Kobenhavn S., DK), Jorgensen, Tino Dyhring; (Solrod Strand, DK), Olesen, Soren Peter; (Klampenborg, DK), Strobaek, Dorte; (Farum, DK), Teuber, Lene; (Varlose, DK)

  Correspondence: Birch Stewart Kolasch & Birch; PO Box 747; Falls Church; VA; 22040-0747; US

  Patent Application Number: 20030114513

  Date filed: October 16, 2002

  Abstract: The present invention relates to ion channel activating agents. More particularly, the present invention relates to a particular class of chemical compounds that has proven useful as openers of SKCa and IKCa channels. In further aspects, the present invention relates to the use of these SK/IK channel activating agents for the manufacture of medicaments and pharmaceutical compositions comprising the SK/IK channel activating agents. The SK/IK channel activating agents of the invention are useful for the treatment or alleviation of diseases and conditions associated with the SK/IK channels, in particular respiratory diseases such as asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory **diarrhea,** ischaemia, cerebral ischaemia, ischaemic heart disease, angina pectoris, coronary heart disease, traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression.

  Excerpt(s): The present invention relates to ion channel activating agents. More particularly, the present invention relates to a particular class of chemical compounds that has proven useful as openers of SK.sub.Ca and IK.sub.Ca channels. In further aspects, the present invention relates to the use of these SK/IK channel activating agents for the manufacture of medicaments, and pharmaceutical compositions comprising the SK/IK channel activating agents. The SK/IK channel activating agents of the invention are useful for the treatment or alleviation of diseases and conditions associated with the SK/IK channels, in particular respiratory diseases such as asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory diarrhoea, ischaemia, cerebral ischaemia, ischaemic hearth disease, angina pectoris, coronary hearth disease, traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labour, baldness, cancer, and immune suppression. Ion channels are transmembrane proteins, which catalyse the transport of inorganic ions across cell membranes. The ion channels participate in processes as diverse as the generation and timing of action potentials, synaptic transmissions, secretion of hormones, contraction of muscles, etc.

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

- **Use of non-digestible polymeric foams to sequester ingested materials thereby inhibiting their absorption by the body**

  Inventor(s): Hird, Bryn; (Cincinnati, OH), Jandacek, Ronald James; (Cincinnati, OH)

  Correspondence: The Procter & Gamble Company; Intellectual Property Division; Winton Hill Technical Center - Box 161; 6110 Center Hill Avenue; Cincinnati; OH; 45224; US

  Patent Application Number: 20030072804

  Date filed: February 26, 2002

  Abstract: This disclosure relates to compositions comprising an open-celled polymeric foam wherein the compositions are useful for sequestering lipophilic materials present in the gastrointestinal tract, thereby inhibiting the absorption of such lipophilic materials by the body. The disclosure further relates to compositions comprising the open-celled polymeric foam wherein the compositions are useful for ameliorating side effects associated with the use of lipase inhibitors. In a preferred embodiment, this disclosure relates to compositions comprising polymeric foam materials made from high internal phase emulsions, where such foams are useful for sequestering lipophilic materials. Further disclosed are compositions comprising open-celled polymeric foams wherein the compositions are useful for the purpose of sequestering aqueous and/or hydrophilic materials present in the gastrointestinal tract, thereby ameliorating **diarrhea.** Kits comprising the compositions and methods of using the compositions and kits are also described.

  Excerpt(s): This application claims priority under Title 35, United States Code 119(e) from Provisional Application Serial No. 60/277,058, filed Mar. 19, 2001. The present invention relates to compositions comprising an open-celled polymeric foam wherein the compositions are useful for sequestering lipophilic materials present in the gastrointestinal tract, thereby inhibiting the absorption of such lipophilic materials by the body. The invention further relates to compositions comprising the open-celled polymeric foam wherein the compositions are useful for ameliorating side effects associated with the use of lipase inhibitors. This invention further relates to compositions comprising an open-celled polymeric foam wherein the compositions are useful for the purpose of sequestering aqueous and/or hydrophilic materials present in the gastrointestinal tract, thereby ameliorating **diarrhea.** This invention additionally relates to kits comprising the compositions and methods of using the compositions and kits. Approximately one third of Americans aged 20 to 74 are considered to be obese, and approximately half of Americans in this age group are considered to be overweight. Obesity is also considered to be a growing problem in other industrialized countries and in developing countries where large numbers of people have become accustomed to Western-influenced high-caloric diets. It has been estimated that obesity contributes to 50% of chronic diseases in Western societies and is responsible for approximately 70% of preventable deaths in the U.S.A. Health care costs associated with obesity are substantial. As a result of these factors, the development of compositions to effect weight-loss is the subject of significant commercial interest.

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

- **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

Keeping Current

In order to stay informed about patents and patent applications dealing with diarrhea, 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 "diarrhea" (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 diarrhea.

You can also use this procedure to view pending patent applications concerning diarrhea. 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 DIARRHEA

Overview

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

- **Diarrheal Diseases**

  Source: New York, NY: Elsevier Science Publishing Company, Inc. 1991. 554 p.

  Contact: Available from Elsevier Science Publishing Company, Inc. Book Order Department, 655 Avenue of the Americas, New York, NY 10010. (212) 989-5800. PRICE: $72. ISBN: 0444015736.

  Summary: This book addresses the subject of diarrheal diseases in a comprehensive manner. It is divided into four sections: the physiology of intestinal fluid transport; the pathophysiology of diarrheal diseases, including the role of inflammatory mediators, virus-gut interactions, how nutrient malabsorption leads to diarrhea, how bacterial enterotoxins cause diarrhea, and the role of motility disorders; a broad spectrum of clinical disease states from congenital diarrheas to ileostomy diarrhea; and therapeutic modalities, including antibiotics, vaccines, oral rehydration therapy, and antidiarrheal

drugs. Each of the 22 chapters contains numerous figures, tables, and references. A detailed subject index is included. 2712 references.

- **Textbook of Secretory Diarrhea**

  Source: New York, NY: Raven Press. 1990. 454 p.

  Contact: Available from Raven Press. 1185 Avenue of the Americas, Dept. 5B, New York, NY 10036. (800) 777-2836 or (212) 930-9500. Fax (212) 869-3495. PRICE: $129 plus shipping (as of 1995). ISBN: 0881676667.

  Summary: This book is a compendium of current knowledge of secretory diarrhea. The authors provide comprehensive coverage of the subject including information on the physiological basis of intestinal transport, the most prevalent clinical features of secretory diarrhea, and therapeutic modalities. Thirty-one chapters, each authored by different experts, are grouped into five sections: regulation of electrolyte and water transport; cellular mechanisms of electrolyte transport by enterocytes; signal transduction through the enterocyte cell membrane; clinical causes of secretory diarrhea, and therapeutic options in secretory diarrhea. A detailed subject index is included. 3539 references.

- **Escherichia Coli 0157:H7: Diarrheal Illness and Hemolytic-Uremic Syndrome**

  Source: Research Triangle Park, NC: Glaxo Wellcome Inc. 1995. 24 p.

  Contact: Available from Glaxo Wellcome Educational Resource Center. 5 Moore Drive, Research Triangle Park, NC 27709. (800) 824-2896. PRICE: Single copy free; available to health care professionals only. Order Number GVL231.

  Summary: This monograph familiarizes readers with diarrheal illness and hemolytic-uremic syndrome (HUS), associated with Escherichia coli 0157:H7. Topics include the epidemiology of illness caused by enterohemorrhagic E. coli, including HUS; methods for isolating and identifying this pathogen and establishing the diagnosis of HUS; treatment for individuals with enterohemorrhagic E. coli-induced illness; and methods for preventing this illness. One section provides information for patients about E. coli 0157:H7. The monograph concludes with a multiple-choice self-test, with which readers can qualify for continuing medical education (CME) credits. 2 figures. 3 tables. 32 references. (AA-M).

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

- **Acute Diarrhea: Its Nutritional Consequences in Children** by Joseph A. Bellanti (Editor); ISBN: 0890049912; http://www.amazon.com/exec/obidos/ASIN/0890049912/icongroupinterna

- **Advances in Research on Cholera and Related Diarrheas: Proceedings of the 18th Joint Conference on** by S. Kuwahara (Editor), N. F. Pierce (Editor) (1985); ISBN: 0898386802;
  http://www.amazon.com/exec/obidos/ASIN/0898386802/icongroupinterna
- **Antibiotic Associated Diarrhea and Colitis: The Role of Clostridium Difficile** by S. Peter Borriello (Editor), Peter S. Borriello (Editor) (1984); ISBN: 0898386233;
  http://www.amazon.com/exec/obidos/ASIN/0898386233/icongroupinterna
- **Bacterial Diarrheal Diseases** by Y. Takeda (Editor) (1985); ISBN: 0898386810;
  http://www.amazon.com/exec/obidos/ASIN/0898386810/icongroupinterna
- **Bile Acids in Health and Disease: Update on Cholesterol, Gallstones and Bile Acid Diarrhea** by Riadh Jazrawi, et al (1988); ISBN: 0746200765;
  http://www.amazon.com/exec/obidos/ASIN/0746200765/icongroupinterna
- **Cholera and Related Diarrheas: Molecular Aspects of a Global Health Problem: (Proceedings of The) 43rd Nobel Symposium, Stockholm, August 6-11, 1978** by J. Holmgren (Editor), et al (1980); ISBN: 3805530609;
  http://www.amazon.com/exec/obidos/ASIN/3805530609/icongroupinterna
- **Chronic Diarrhea in Children (Nestle Nutrition Workshop Series; V. 6)** by Emanuel Lebenthal (Editor); ISBN: 0890043191;
  http://www.amazon.com/exec/obidos/ASIN/0890043191/icongroupinterna
- **Cumitechs 12a Laboratory Diagnosis of Bacterial Diarrhea** (1992); ISBN: 9992264535;
  http://www.amazon.com/exec/obidos/ASIN/9992264535/icongroupinterna
- **Diarrhea** by Michael Gracey (Contributor), Espinoza (Contributor); ISBN: 0849388198;
  http://www.amazon.com/exec/obidos/ASIN/0849388198/icongroupinterna
- **Diarrhea and Malnutrition in Childhood** by J.A. Walker-Smith, A.S. McNeish; ISBN: 0407004017;
  http://www.amazon.com/exec/obidos/ASIN/0407004017/icongroupinterna
- **Diarrhea and Malnutrition: Interactions, Mechanisms and Interventions** by Lincoln C. and Scrimshaw, Nevin S. Chen (Editor); ISBN: 030641046X;
  http://www.amazon.com/exec/obidos/ASIN/030641046X/icongroupinterna
- **Diarrhea, Diarrhea: And Other School Poems for Children** by Sigmund A. Boloz, et al (1998); ISBN: 1886635153;
  http://www.amazon.com/exec/obidos/ASIN/1886635153/icongroupinterna
- **Diarrheal Disease (Nestle Nutrition Workshop Series, Vol. 38)** by Michael Gracey (Editor), et al; ISBN: 0397587716;
  http://www.amazon.com/exec/obidos/ASIN/0397587716/icongroupinterna
- **Diarrheal Disease and Malnutrition: A Clinical Update** by Michael Gracey (Editor); ISBN: 0443028923;
  http://www.amazon.com/exec/obidos/ASIN/0443028923/icongroupinterna
- **Diarrheal Diseases** (1991); ISBN: 0444015736;
  http://www.amazon.com/exec/obidos/ASIN/0444015736/icongroupinterna
- **Diarrheal Diseases (Current Topics in Gastroenterology)** by Michael Field (Editor); ISBN: 083851684X;
  http://www.amazon.com/exec/obidos/ASIN/083851684X/icongroupinterna
- **Healthy Digestion the Natural Way: Preventing and Healing Heartburn, Constipation, Gas, Diarrhea, Inflammatory Bowel and Gallbladder Diseases, Ulcers,**

Irritable Bowel Syndrome, and More by D. Lindsey Berkson (Author); ISBN: 0471349623; http://www.amazon.com/exec/obidos/ASIN/0471349623/icongroupinterna

- **Infectious Diarrhea** by Sherwood L. Gorbach (Editor); ISBN: 0801619076; http://www.amazon.com/exec/obidos/ASIN/0801619076/icongroupinterna
- **Infectious diarrhea**; ISBN: 0865420300; http://www.amazon.com/exec/obidos/ASIN/0865420300/icongroupinterna
- **Infectious Diarrhea in the Young: Strategies for Control in Humans and Animals (International Congress Series, 674)** by Saul Tzipori (Editor); ISBN: 0444807209; http://www.amazon.com/exec/obidos/ASIN/0444807209/icongroupinterna
- **Infectious Diarrheal Diseases: Current Concepts and Laboratory Procedures** by Paul D. Ellner (Editor); ISBN: 082477129X; http://www.amazon.com/exec/obidos/ASIN/082477129X/icongroupinterna
- **Laboratory Diagnosis in Neonatal Calf and Pig Diarrhea. Ed by P.W. De Leeuw. Result of Eec Meeting Held Lelystad, the Netherlands, 1980: Proceedings of a Workshop on Diagnostic Techniques for Enteropathogenic Agents Associated With Neonatal Diarrhoea in Calves and Pigs, Held at the (Current Topics in Veterinary Medicine and Animal Science, V. 13)** by Workshop on Diagnostic Techniques for Enteropathogenic Agents Associat, et al (1981); ISBN: 9024725275; http://www.amazon.com/exec/obidos/ASIN/9024725275/icongroupinterna
- **Malnutrition in Chronic Diet-Associated Infantile Diarrhea: Diagnosis and Management (Bristol-Myers Squibb/Mead Johnson Nutrition Symposia, Vol. 8)** by Carlos H. Lifschitz, Buford L. Nichols (Editor); ISBN: 012450020X; http://www.amazon.com/exec/obidos/ASIN/012450020X/icongroupinterna
- **Microbial Toxins and Diarrheal Disease (Ciba Foundation Symposium 112)** by David Evered, Julie Whelan (Editor); ISBN: 0471910813; http://www.amazon.com/exec/obidos/ASIN/0471910813/icongroupinterna
- **Mikwright Come on In! I'm Sorry, But Robert's Got Diarrhea and the Kids Both Have Lice, So. It's J** by MikWright Ltd (2003); ISBN: 0740707922; http://www.amazon.com/exec/obidos/ASIN/0740707922/icongroupinterna
- **Nutrition Issues in Developing Countries: Part I: Diarrheal Diseases: Part II: Diet and Activity During Pregnancy and Lactation** by Institute of Medicine, Subcommittee on Nutrition & Diarrheal Co (Editor) (1992); ISBN: 0309040922; http://www.amazon.com/exec/obidos/ASIN/0309040922/icongroupinterna
- **Physicians' Guide to the Etiology and Treatment of Diarrhea** by Horacio Jinich, Theodoro Hersh; ISBN: 0874892686; http://www.amazon.com/exec/obidos/ASIN/0874892686/icongroupinterna
- **Preventing Travelers' Diarrhea (Nuts 'N' Bolts Guide)** by Donald Sullivan; ISBN: 0897321766; http://www.amazon.com/exec/obidos/ASIN/0897321766/icongroupinterna
- **Reducing Diarrhea in Tube-Fed Patients (Using Research to Improve Nursing Practice)** by Jo Anne Horsley; ISBN: 0808913263; http://www.amazon.com/exec/obidos/ASIN/0808913263/icongroupinterna
- **Secretory diarrhea**; ISBN: 0683032011; http://www.amazon.com/exec/obidos/ASIN/0683032011/icongroupinterna

- **Secretory Diarrhea** by Michael Field (Editor), et al; ISBN: 0195206932; http://www.amazon.com/exec/obidos/ASIN/0195206932/icongroupinterna
- **Sociocultural factors influencing the prevalence of diarrheal disease in rural Upper Egypt : an ethnographic study in six villages : final summary report** by Linda Oldham; ISBN: 9280600478; http://www.amazon.com/exec/obidos/ASIN/9280600478/icongroupinterna
- **Sociocultural factors influencing the prevalence of diarrheal disease in rural Upper Egypt : an ethnographic study in two villages of Aswan : final report submitted to UNICEF** by Saneya Wahba; ISBN: 9280600508; http://www.amazon.com/exec/obidos/ASIN/9280600508/icongroupinterna
- **Sociocultural factors influencing the prevalence of diarrheal disease in rural Upper Egypt : an ethnographic study in two villages of Sohag : final report submitted to UNICEF** by Hajir Hadidi; ISBN: 9280600494; http://www.amazon.com/exec/obidos/ASIN/9280600494/icongroupinterna
- **Synthetic antidiarrheal drugs : synthesis--preclinical and clinical pharmacology**; ISBN: 082476370X; http://www.amazon.com/exec/obidos/ASIN/082476370X/icongroupinterna
- **Textbook of Secretory Diarrhea** by Emanuel Lebenthal, Michael E. Duffey (Editor); ISBN: 0881676667; http://www.amazon.com/exec/obidos/ASIN/0881676667/icongroupinterna
- **The 2002 Official Patient's Sourcebook on Diarrhea: A Revised and Updated Directory for the Internet Age** by Icon Health Publications (2002); ISBN: 0597832668; http://www.amazon.com/exec/obidos/ASIN/0597832668/icongroupinterna
- **The 30-Day Diarrhea Diet Plan** by Kurt P Brecht (1989); ISBN: 1879188015; http://www.amazon.com/exec/obidos/ASIN/1879188015/icongroupinterna
- **The Evaluation and Treatment of the Patient With Diarrhea** by Paul F. Miskovitz, Arnold M. Rochwarger; ISBN: 1563720590; http://www.amazon.com/exec/obidos/ASIN/1563720590/icongroupinterna
- **The Management and Prevention of Diarrhea: Practical Guidelines** by World Health Organization Staff (Editor), World Health Organization (Editor) (1993); ISBN: 9241544546; http://www.amazon.com/exec/obidos/ASIN/9241544546/icongroupinterna
- **The Official Patient's Sourcebook on Chronic Diarrhea: A Revised and Updated Directory for the Internet Age** by Icon Health Publications (2002); ISBN: 0597834229; http://www.amazon.com/exec/obidos/ASIN/0597834229/icongroupinterna
- **The Official Patient's Sourcebook on Travelers' Diarrhea** by James N. Parker, Health Publica Icon Health Publications; ISBN: 0597829748; http://www.amazon.com/exec/obidos/ASIN/0597829748/icongroupinterna
- **The Rational Use of Drugs in the Management of Acute Diarrhea in Children** (1987); ISBN: 9241561424; http://www.amazon.com/exec/obidos/ASIN/9241561424/icongroupinterna
- **Traveler's Diarrhea: Recent Advances ('Chemotherapy', Vol 41, Supplement 1)** by C. Scarpignato, P. Rampal (Editor) (1995); ISBN: 3805561253; http://www.amazon.com/exec/obidos/ASIN/3805561253/icongroupinterna
- **Traveller's Diarrhea** by Charles D., Md. Ericsson, et al (2003); ISBN: 1550092197; http://www.amazon.com/exec/obidos/ASIN/1550092197/icongroupinterna

- **Viral Diarrheas of Man and Animals** by Linda J. Saif, et al; ISBN: 0849366402; http://www.amazon.com/exec/obidos/ASIN/0849366402/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 "diarrhea" (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:[11]

- **Chronic and recurrent diarrhea.** Author: Almy, Thomas Pattison,; Year: 1954; Chicago, Year Book Publishers, 1955
- **Chronic diarrhea** Author: Gryboski, Joyce D.,; Year: 1972; Chicago: Year Book Medical Publishers, 1979
- **Clinical experience with selective gastric and total abdominal vagotomy; special reference to insulin test and postvagotomy diarrhea.** Author: Inberg, M. V.; Year: 1964; Turku, 1969
- **Conference on epidemic diarrhea among newborns, August 27, 1946, Leland Hotel, Springfield, Illinois.** Author: Illinois. Dept. of Public Health.; Year: 1971; [Springfield, 1946]
- **Diarrheal disease and oral rehydration: an annotated bibliography** Author: Baumslag, Naomi.; Year: 1958; Washington: Office of International Health, U. S. D. H. E. W., 1979
- **Evaluation of the electron microscopic and adrenal cell assays in determining the etiology of infectious diarrhea in Rochester children** Author: Taraska, Stanley P.; Year: 1961; [Minneapolis?: s.n.], 1978
- **Field procedures for bacteriological studies of diarrheal diseases, by Don C. Mackel.** Author: Communicable Disease Center (U.S.). Technology Branch.; Year: 1965; Phoenix, Ariz. [1964]
- **Isolation and identification of Escherichia coli serotypes association with diarrheal diseases.** Author: Ewing, William H. (William Howell),; Year: 1965; Atlanta, U. S. Communicable Disease Center, Laboratory Branch, 1963
- **Proctoscopic examination and diagnosis and treatment of diarrheas.** Author: Streicher, Michael Henry,; Year: 1963; Springfield, Ill., C. C. Thomas [c1940]
- **Studies on the occurrence of Escherichia coli serotypes associated with diarrheal disease [by] W. H. Ewing [et al.].** Author: Ewing, William H. (William Howell),; Year: 1968; Atlanta, U. S. Communicable Disease Center, Laboratory Branch, 1963
- **The diagnosis and treatment of diarrheal diseases.** Author: Fradkin, William Zev,; Year: 1933; New York, Grune; Stratton, 1947

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[11] 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**.

- **The differential diagnosis of diarrhea.** Author: Mellinkoff, Sherman M. (Sherman Mussoff),; Year: 1963; New York, McGraw-Hill [c1964]
- **The intestinal tract in diabetes mellitus with particular reference to diabetic diarrhea; a pathologic study.** Author: Berge, Kenneth George.; Year: 1964; [Minneapolis] 1955

Chapters on Diarrhea

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

- **Infectious Diarrhea and Bacterial Food Poisoning**

  Source: in Feldman, M.; Friedman, L.S.; Sleisenger, M.H. Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management. 7th ed. [2-volume set]. St. Louis, MO: Saunders. 2002. p. 1864-1913.

  Contact: Available from Elsevier. 11830 Westline Industrial Drive, St. Louis, MO 63146. (800) 545-2522. Fax (800) 568-5136. Website: www.us.elsevierhealth.com. PRICE: $229.00 plus shipping and handling. ISBN: 0721689736.

  Summary: This chapter on infectious diarrhea and bacterial food poisoning is from a comprehensive and authoritative textbook that covers disorders of the gastrointestinal tract, biliary tree, pancreas, and liver, as well as the related topics of nutrition and peritoneal disorders. Topics include changes in normal flora caused by diarrhea; classification of bacterial diarrhea; toxigenic diarrheas, including cholera, other vibrios, Aeromonas, Plesiomonas shigelloides, and Escherichia coli; invasive pathogens, including Shigella, nontyphoidal Salmonellosis, typhoid fever, Campylobacter, and Yersinia; viral diarrhea, including that due to rotavirus, calicivirus, enteric andenovirus, astrovirus, and torovirus; traveler's diarrhea, including microbiology, epidemiology, clinical features, and prevention; diarrhea in the elderly; diagnosis of infectious diarrheal disease; treatment of infectious diarrhea, including with fluid therapy, diet, antimicrobial drugs, and nonspecific therapy; tuberculosis of the gastrointestinal tract; and bacterial food poisoning, including that from Clostridium perfringers, Saphylococcus auerus, Listeria, Bacillus cereus, botulism, and Bacillus anthracis. The chapter includes a mini-outline with page citations, illustrations, and extensive references. 8 figures. 16 tables. 329 references.

- **Approach to the Patient with Diarrhea**

  Source: in Textbook of Gastroenterology. 4th ed. [2-volume set]. Hagerstown, MD: Lippincott Williams and Wilkins. 2003. p. 844-894.

  Contact: Available from Lippincott Williams and Wilkins. P.O. Box 1600, Hagerstown, MD 21741. (800) 638-6423. Fax: (301) 223-2400. Website: www.lww.com. PRICE: $289.00. ISBN: 781728614.

Summary: This chapter on the approach to patients with diarrhea is from a lengthy, two-volume textbook that integrates the various demands of science, technology, expanding information, good judgment, and common sense into the diagnosis and management of gastrointestinal patients. Topics include general epidemiology, general definition, pathophysiology of diarrhea, a definition of acute diarrhea, acute infectious diarrheas, prolonged infectious diarrheas, nosocomial diarrheas, runner's diarrhea, chronic diarrheas, steatorrhea (malabsorptive diseases), watery diarrheas, true secretory diarrheas, inflammatory diarrheas, the clinical evaluation of chronic diarrhea, and antidiarrheal therapy. 11 figures. 16 tables. 574 references.

- **Diarrhea in Children: A Historical Review**

  Source: in Chen, T.S., and Chen, P.S., eds. History of Gastroenterology: Essays on Its Development and Accomplishments. New York, NY: Parthenon Publishing Group, Inc. 1995. p. 201-215.

  Contact: Available from Parthenon Publishing. 1 Blue Hill Plaza, P.O. Box 1564, Pearl River, NY 10965. (800) 735-4744 or (914) 735-9363. Fax (914) 735-1385. PRICE: $88.00 (as of 1996). ISBN: 1850703655.

  Summary: This chapter, from a compilation of essays that relate the emergence and history of the field of gastroenterology, presents a historical review of diarrhea in children. Topics include the early recognition of the severity of diarrhea in children, early therapeutic recommendations, the medical thought surrounding diarrhea from ancient Rome into the 19th century, etiologic considerations, the impact of the science of bacteriology on the subject of childhood diarrhea, the introduction of mandatory milk pasteurization, the clinical and bacteriologic studies of the 19th century, and the concept of acidosis. This paper was originally published in 1960. 2 tables. 103 references.

- **Nutrition Management of Diarrhea in Childhood**

  Source: in American Dietetic Association. Manual of Clinical Dietetics. Chicago, IL: American Dietetic Association. 1996. p. 237-246.

  Contact: Available from American Dietetic Association. 216 West Jackson Boulevard, Chicago, IL 60606. (800) 877-1600 or (312) 899-0040. Fax (312) 899-4899. PRICE: $59.95 for members, $70.00 for nonmembers. ISBN: 0880911530.

  Summary: This section on the nutrition management of diarrhea in childhood is from a manual that serves as a nutrition care guide for dietetics professionals, physicians, nurses, and other health professionals. The manual integrates current knowledge of nutrition, medical science, and food to set forth recommendations for healthy individuals and those for whom medical nutrition therapy (MNT) is indicated. This section outlines guidelines for the three classifications of diarrhea seen in childhood (acute; protracted; or chronic, nonspecific). The guidelines are intended to help alleviate symptoms and to prevent the complications of dehydration, weight loss, and growth failure. The text notes the purpose, use, modifications, and adequacy of the diets. Topics include rehydration phase guidelines, the maintenance phase, reintroducing previous diet, breast-fed infants, formula-fed infants, parenteral and enteral requirements, and issues of adequacy. 1 table. 36 references. (AA-M).

- **Acute Diarrhea in Adults**

  Source: in Edmundowicz, S.A., ed. 20 Common Problems in Gastroenterology. New York, NY: McGraw-Hill, Inc. 2002. p. 159-176.

Contact: Available from McGraw-Hill, Inc. 1221 Avenue of the Americas, New York, NY 10020. (612) 832-7869. Website: www.bookstore.mcgraw-hill.com. PRICE: $45.00;plus shipping and handling. ISBN: 0070220557.

Summary: Acute diarrhea is an increase in stool liquidity or a decrease in consistency, often associated with an increase in stool frequency and volume compared with the patient's usual bowel habits. Diarrhea persisting beyond 4 weeks is regarded as chronic. This chapter on acute diarrhea in adults is from a book that focuses on the most common gastroenterological problems encountered in a primary practice setting. The chapter is organized to support rapid access to the information necessary to evaluate and treat most patients with this problems. Topics include definition and epidemiology; the general approach to patients with acute diarrhea; key history and physical examination points; ancillary tests, including stool examination, stool ova (eggs) and parasite examination; infectious agents, including viral diarrheas, bacterial diarrhea, toxin-induced diarrhea, inflammatory diarrhea due to invasive organisms, parasitic diseases, hospital-acquired diarrhea, traveler's diarrhea, diarrhea in the immunocompromised host, medications as a cause of diarrhea, idiopathic inflammatory bowel disease (IBD), diarrhea in runners, alcohol-induced diarrhea, and the emergence of new diarrheal syndromes and pathogens; patient management, including fluid and electrolyte replacement and food restriction; medications, including adsorbents, antimotility agents, antimicrobials, and antiemetics; patient education; and emerging concepts and controversies. The chapter includes an outline for quick reference, the text itself, a diagnostic and treatment algorithm, and selected references. 1 figure. 9 tables. 25 references.

- **Persistent Diarrheal Disease**

Source: Kleinmann, R.E., ed. Pediatric Nutrition Handbook. 4th ed. Elk Grove Village, IL: American Academy of Pediatrics. 1998. p. 337-350.

Contact: Available from American Academy of Pediatrics. P.O. Box 927, 141 Northwest Point Boulevard, Elk Grove Village, IL 60009-0927. (800) 433-9016. PRICE: $47.95 (members) plus $6.25 shipping and handling; $52.95 for nonmembers; plus $8.95 shipping and handling. ISBN: 1581100051.

Summary: Assessment of nutritional status and providing dietary advice and nutritional support are important and increasingly prominent components of the practice of those who provide health care for infants, children, and adolescents. This chapter on persistent diarrheal disease is from a handbook that serves as a ready desk reference on the nutritional requirements and impact of nutritional status on the health of infants, children, and adolescents. Persistent (or chronic) diarrhea is defined by the World Health Organization as any episode of diarrhea that lasts longer than 2 weeks. Persistent diarrhea can be the end result of disorders of intestinal motility, maldigestion, malabsorption, or intestinal inflammation. Topics include the evaluation of the infant and child with persistent diarrhea, including history, physical examination, macroscopic and microscopic examination of the stool, examination for fecal carbohydrate, bacterial cultures, sweat chloride, fecal fat, immunoelectrophoresis, tolerance tests, roentgenograms, and invasive procedures (including endoscopy and intestinal biopsy); disorders of motility, including chronic nonspecific diarrhea (toddler's diarrhea); disorders of digestion, including exocrine pancreatic insufficiency (EPI, including cystic fibrosis) and lactose intolerance; disorders of absorption, including celiac disease (gluten-sensitive enteropathy), postgastroenteritis syndrome with persistent diarrhea and malabsorption, short bowel syndrome, and inflammatory bowel disease (IBD, which includes Crohn's disease and ulcerative colitis). 14 references.

- **Secretory Diarrhea**

  Source: in Brandt, L., et al., eds. Clinical Practice of Gastroenterology. Volume One. Philadelphia, PA: Current Medicine. 1999. p. 615-625.

  Contact: Available from W.B. Saunders Company. Order Fulfillment, 6277 Sea Harbor Drive, Orlando, FL 32887. (800) 545-2522. Fax (800) 874-6418 or (407) 352-3445. Website: www.wbsaunders.com. PRICE: $235.00 plus shipping and handling. ISBN: 0443065209 (two volume set); 0443065217 (volume 1); 0443065225 (volume 2).

  Summary: Clinical investigators broadly categorize diarrhea as secretory or osmotic, by measuring electrolytes and the osmolality of fecal fluid. In secretory diarrheas, analysis of the fecal fluid reveals that sodium, potassium, and accompanying anions account entirely for the observed osmolarity. This chapter on secretory diarrhea is from a lengthy textbook that brings practitioners up to date on the complexities of gastroenterology practice, focusing on the essentials of patient care. The author of this chapter reassesses the clinical and basic models of secretory diarrheas and considers how relevant they may be to the realities of clinical practice. Acute diarrheas may have a secretory component, but in Western countries, they are generally transient and rarely life threatening conditions, except perhaps in infants. Despite the vast array of diagnostic studies that can be used to evaluate a complaint of chronic diarrhea, making a specific diagnosis is often difficult. The basic and clinical models of secretory diarrhea in use have been shaped by the medical understanding of cholera. A focused and orderly workup of the patient can assist in understanding the pathophysiology, and then one can begin appropriate treatment. However, the symptoms of diarrhea can often be controlled adequately without altering the primary pathophysiologic abnormality. Patients can be placed on a therapeutic trial with loperamide or diphenoxylate. Although patients often take these drugs sporadically with some success, a regular dosing schedule may provide significant amelioration of symptoms. 5 figures. 5 tables. 36 references.

- **Infectious Diarrhea**

  Source: in Brandt, L., et al., eds. Clinical Practice of Gastroenterology. Volume One. Philadelphia, PA: Current Medicine. 1999. p. 527-535.

  Contact: Available from W.B. Saunders Company. Order Fulfillment, 6277 Sea Harbor Drive, Orlando, FL 32887. (800) 545-2522. Fax (800) 874-6418 or (407) 352-3445. Website: www.wbsaunders.com. PRICE: $235.00 plus shipping and handling. ISBN: 0443065209 (two volume set); 0443065217 (volume 1); 0443065225 (volume 2).

  Summary: Diarrheal illnesses are among the most common infectious diseases in the developed and developing world, and they are important causes of significant morbidity and mortality. This chapter on infectious diarrhea is from a lengthy textbook that brings practitioners up to date on the complexities of gastroenterology practice, focusing on the essentials of patient care. The author of this chapter reviews the most important acute infectious diarrheal diseases, emphasizing their diagnostic features and management. The morbidity and mortality attributable to diarrheal illnesses is age specific; in children, diarrhea is second only to acute respiratory complaints as the most frequent reason for physician visits. Diarrhea associated mortality in the United States is highest for the elderly, but children account for most deaths in developing countries. Several host (i.e., altered host defenses) and microbial factors play roles in the development of diarrhea. To assess the need for and level of intervention, the physician must obtain a careful history, including food intake and travel. Diarrheal syndromes are discussed in categories: watery diarrhea syndromes, dysentery syndromes, invasive

diarrhea syndromes, and diarrheal syndromes in immunocompromised hosts (discussed in detail in another chapter of the text). In each category, the author reviews clinical features, the major pathogens, and treatment options. An algorithm is provided for the evaluation of acute infectious diarrhea. 3 figures. 6 tables. 26 references.

- **Tropical Malabsorption and Tropical Diarrhea**

  Source: in Feldman, M.; Friedman, L.S.; Sleisenger, M.H. Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management. 7th ed. [2-volume set]. St. Louis, MO: Saunders. 2002. p. 1842-1853.

  Contact: Available from Elsevier. 11830 Westline Industrial Drive, St. Louis, MO 63146. (800) 545-2522. Fax (800) 568-5136. Website: www.us.elsevierhealth.com. PRICE: $229.00 plus shipping and handling. ISBN: 0721689736.

  Summary: Malabsorption of dietary nutrients by the small intestine has special relevance for people living in the tropics and subtropics. The causes of intestinal malabsorption differ from those commonly seen in the industrialized world, and the clinical impact is often substantially greater because many persons in the developing world, particularly infants and young children, often exist in a state of borderline undernutrition. Tropical malabsorption can be caused either by specific causes, such as infections of known etiology and inflammatory and neoplastic disorders, or nonspecific conditions, such as tropical enteropathy and tropical sprue, for which the etiology has not been determined. This chapter on tropical malabsorption and tropical diarrhea is from a comprehensive and authoritative textbook that covers disorders of the gastrointestinal tract, biliary tree, pancreas, and liver, as well as the related topics of nutrition and peritoneal disorders. Topics include specific causes of tropical malabsorption, including intestinal infection, celiac sprue, lymphoma, severe undernutrition, and primary hypolactasia; nonspecific tropical malabsorption; the definition, epidemiology, pathophysiology, and theories of pathogenesis of tropical enteropathy; and the definition, historical aspects, epidemiology, clinical features, pathology, pathophysiology, pathogenesis, diagnosis, treatment, and prevention of tropical sprue. The chapter includes a mini-outline with page citations, illustrations, and extensive references. 7 figures. 2 tables. 171 references.

- **Pseudomembranous Enterocolitis and Antibiotic-Associated Diarrhea**

  Source: in Feldman, M.; Friedman, L.S.; Sleisenger, M.H. Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management. 7th ed. [2-volume set]. St. Louis, MO: Saunders. 2002. p. 1914-1931.

  Contact: Available from Elsevier. 11830 Westline Industrial Drive, St. Louis, MO 63146. (800) 545-2522. Fax (800) 568-5136. Website: www.us.elsevierhealth.com. PRICE: $229.00 plus shipping and handling. ISBN: 0721689736.

  Summary: Pseudomembranous enterocolitis is characterized by gross or histologic evidence of pseudomembranous exudative plaques attached to the mucosal surface of the small intestine, colon, or both. The vast majority of cases reported during the past three decades have occurred in association with antibiotic exposure. This chapter on pseudomembranous enterocolitis and antibiotic-associated diarrhea is from a comprehensive and authoritative textbook that covers disorders of the gastrointestinal tract, biliary tree, pancreas, and liver, as well as the related topics of nutrition and peritoneal disorders. Topics include an historical perspective; pathology; underlying and associated conditions; clinical features; pathophysiology, including colonization rates, in vitro susceptibility, epidemiology, Clostridium difficile toxins, age-related risk,

and immunologic susceptibility; diagnostic considerations; treatment options, including antibiotics, relapses, surgery, and infection control; and prevention. The chapter includes a mini-outline with page citations, illustrations, and extensive references. 7 figures. 5 tables. 259 references.

- **Irritable Bowel Syndrome and Diarrhea**

  Source: in Snape, W.J., ed. Consultations in Gastroenterology. Philadelphia, PA: W.B. Saunders Company. 1996. p. 502-510.

  Contact: Available from W.B. Saunders Company. Order Fulfillment, 6277 Sea Harbor Drive, Orlando, FL 32887. (800) 545-2522. Fax (800) 874-6418 or (407) 352-3445. PRICE: $125.00. ISBN: 0721646700.

  Summary: This chapter from a gastroenterology text covers irritable bowel syndrome (IBS) and diarrhea. The IBS is a heterogeneous group of functional gastrointestinal tract disorders involving the small intestine and colon; central to the definition of IBS is abdominal pain. The authors first provide some background regarding aspects of the history, physical examination, and initial laboratory evaluation that supports the diagnosis of this common presentation. The authors caution against performing excessive diagnostic tests, which can undermine the patient's confidence in both the physician and the diagnosis, as well as play into the tendency of patients with IBS to seek opinions from multiple physicians. The authors also discuss the psychosocial support that is an important component in the management of a chronic disorder such as IBS. They recommend establishing early in the treatment plan a realistic goal of reducing and not eradicating symptoms, emphasizing that the physician and patient share responsibility for management decisions. Treatment options discussed include diet and bulking agents, opiates, anticholinergics, antispasmodics, peppermint oil, calcium channel blockers, allergy medicine, anxiolytics and antidepressants, and peptides and biogenic amines. 1 figure. 2 tables. 49 references.

- **Antidiarrheals**

  Source: in Moreau, D., ed. Nursing96 Drug Handbook. Springhouse, PA: Nursing96 Books. Springhouse Corporation. 1996. p. 633-640.

  Contact: Available from Springhouse Publishing. 1111 Bethlehem Pike, P.O. Box 908, Springhouse, PA 19477. (800) 331-3170 or (215) 646-4670 or (215) 646-4671. Fax (215) 646-8716. PRICE: $29.95. ISBN: 087434817X. ISSN: 0273320x.

  Summary: This chapter on antidiarrheals is from a nursing handbook on pharmaceuticals. The handbook is designed to provide drug information that focuses on what nurses need to know by emphasizing the clinical aspects of drug therapy. The chapter begins with an alphabetical list of the generic names of drugs described in the chapter, followed by an alphabetized list of its brand names. Finally comes a list of selected combination products in which these drugs are found. Specific information on each drug is arranged under the following headings: How Supplied, Action, Onset, Peak, Duration, Indications and Dosage, Adverse Reactions, Interactions, Contraindications, and Nursing Considerations. Drugs covered are bismuth subgallate, bismuth subsalicylate, clacium polycarbophil, difenoxin hydrochloride and atropine sulfate, kaolin and pectin mixtures, loperamide, octreotide acetate, opium tincture, and camphorated opium tincture.

- **Diarrhea and Constipation**

  Source: in Janowitz, H.D. Good Food for Bad Stomachs. New York, NY: Oxford University Press. 1997. p. 110-127.

  Contact: Available from Oxford University Press. Order Department, 2001 Evans Road, Cary, NC 27513. (800) 451-7556. Fax (919) 677-1303. PRICE: $12.95 plus shipping and handling. ISBN: 0195126556.

  Summary: This chapter on diarrhea and constipation is from a book that presents a detailed look at present knowledge about the role of eating habits in preventing, causing, and treating the many disorders that plague the gastrointestinal tract and its associated digestive glands, the liver, the gallbladder, and the pancreas. Diarrhea is defined as bowel movements that occur too often and are too loose, constipation as difficulty in moving one's bowels. To put these definitions into proper perspective, the author notes that the number of bowel movements that normal people in good health can pass varies tremendously, ranging from two to three a day to two to three a week. Therefore, instead of comparing themselves with others, people should look for deviations from their ordinary routines both in number and consistency of the stool. Topics include acute diarrhea, its symptoms, causes, and treatment; what to eat during acute episodes of diarrhea; food poisoning; traveler's diarrhea and how to avoid it; parasites in the stool; secretory diarrhea; food intolerance as a cause of diarrhea; antibiotic associated diarrhea; constipation, its causes and treatments; the role of dietary fiber and treatment with a high fiber diet; the unique role of bran; lubricants; enemas; and fluid intake. 2 tables.

- **Diarrhea Following Small Bowel Resection**

  Source: in Bayless, T.M. and Hanauer, S.B. Advanced Therapy of Inflammatory Bowel Disease. Hamilton, Ontario: B.C. Decker Inc. 2001. p. 471-474.

  Contact: Available from B.C. Decker Inc. 20 Hughson Street South, P.O. Box 620, L.C.D. 1 Hamilton, Ontario L8N 3K7. (905) 522-7017 or (800) 568-7281. Fax (905) 522-7839. Email: info@bcdecker.com. Website: www.bcdecker.com. PRICE: $129.00 plus shipping and handling. ISBN: 1550091220.

  Summary: This chapter on diarrhea following small bowel resection (removal) for Crohn's disease is from the second edition of a book devoted to the details of medical, surgical, and supportive management of patients with Crohn's disease (CD) and ulcerative colitis (UC), together known as inflammatory bowel disease (IBD). In intestinal diseases, such as CD and colitis, the normal orderly process of absorption is disrupted, and malabsorption of fluid and electrolytes may cause diarrhea. These intestinal diseases also may result in nutrient malabsorption and the consequences of malnutrition. Intestinal resection permanently removes one or more segments of the intestine. The extent of the absorptive defect depends upon which segment has been removed, how extensive the resection has been, and the ability of other segments to compensate for the missing functions of that segment. Diarrhea can develop shortly after recovery from surgery and refeeding, or some time after recovery from surgery. The time of onset after surgery is an important clue to the possible cause of the diarrhea, thus, careful patient history is crucial for appropriate diagnosis. If a specific problem, such as bacterial overgrowth, is identified, specific treatment can be applied and may substantially improve the situation. Often a specific treatable entity cannot be diagnosed and nonspecific treatment must be applied. Nonspecific treatment can provide significant improvement in symptoms and allow for use of the absorptive surface of the intestine in a more efficient fashion. Nonspecific treatments include diet therapy

(reduction in fat intake, frequent feedings, dietary supplements, reduced caffeine intake); antidiarrheal medications; stool modifying agents; adjunctive medications; and replacement therapy (oral rehydration solution, vitamins). 4 tables. 8 references.

Directories

In addition to the references and resources discussed earlier in this chapter, a number of directories relating to diarrhea have been published that consolidate information across various sources. The Combined Health Information Database lists the following, which you may wish to consult in your local medical library:[12]

- **Directory of Plain Language Health Information**

  Source: Ottawa, Ontario: Canadian Public Health Association. 1999. 104 p.

  Contact: Available from Canadian Public Health Association. 400-1565 Carling Avenue, Ottawa, Ontario, K1Z 8R1. (613) 725-3769. Fax (613) 725-9826. E-mail: comm@cpha.ca. PRICE: $19.95 plus shipping and handling. Also available at www.pls.cpha.ca for free. ISBN: 189432403X.

  Summary: Patient education materials are often written at a level that is higher than the reading level of the people who need the materials. This directory lists 'plain language' patient education materials. An extensive introductory chapter in the directory describes how patient education materials are evaluated and offers specific information about the best strategies to create plain language materials. Each piece of health information in the directory is rated according to its design assessment, in order to help readers make informed decisions about choosing materials. Part I is a list of health subjects presented in alphabetical order, in the style of a typical index. The page number after a listing notes where to find that piece of health information in Part II. Part II is a list of organizations and their contact information. Below the contact information is a list of the plain language health titles produced by the organization. Each title is grouped under a grade level heading, is numbered, and has a design rating. Part III is an alphabetical list of all the organizations in Part II. Materials related to digestive system diseases include allergies, constipation and soiling in children, cholesterol, hepatitis, constipation, diabetes and diet therapy, exercise for weight control, food choices, nutrition, heart health, immunization, low fat cooking, nausea, vomiting, **diarrhea,** smoking, and weight loss. Appendices to the directory include a guide to the S.M.O.G. readability formula, clear design tips, and plain language tips. The Directory is also available at www.pls.cpha.ca on the Internet.

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[12] You will need to limit your search to “Directory” and “diarrhea” using the "Detailed Search" option. Go directly to the following hyperlink: **http;//chid.nih.gov/detail/detail.html**. To find directories, use the drop boxes at the bottom of the search page where “You may refine your search by.” For publication date, select “All Years.” Select your preferred language and the format option “Directory.” Type “diarrhea” (or synonyms) into the “For these words:” box. You should check back periodically with this database as it is updated every three months.

CHAPTER 8. MULTIMEDIA ON DIARRHEA

Overview

In this chapter, we show you how to keep current on multimedia sources of information on diarrhea. We start with sources that have been summarized by federal agencies, and then show you how to find bibliographic information catalogued by the National Library of Medicine.

Video Recordings

An excellent source of multimedia information on diarrhea is the Combined Health Information Database. You will need to limit your search to "Videorecording" and "diarrhea" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find video productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Videorecording (videotape, videocassette, etc.)." Type "diarrhea" (or synonyms) into the "For these words:" box. The following is a typical result when searching for video recordings on diarrhea:

- **Approach to the Patient with Chronic Diarrhea**

  Source: Secaucus, NJ: Network for Continuing Medical Education (NCME). 1993.

  Contact: Available from NCME. One Harmon Plaza, Secaucus, NJ 07094. (800) 223-0272 or, in New Jersey, (800) 624-2102, or (201) 867-3550. PRICE: $20 for 2-week rental or $50 for purchase. Available only to NCME subscribers; subscriber fees as of 1995 are $1,920 for VHS subscription, $2,120 for U-matic subscription.

  Summary: In this continuing education program, Dr. Asher Kornbluth guides viewers through the approach to the patient with chronic diarrhea. In the first section, Dr. Kornbluth presents a definition of chronic diarrhea, emphasizes the importance of obtaining a comprehensive, accurate patient history, and reviews the categories of chronic diarrhea, including altered motility, osmotic, inflammatory, secretory, and factitious. He briefly reviews conditions that may cause fecal incontinence, including advanced age, diabetes, and neuromuscular disease, and comments on HIV-associated diarrhea. In the second section, he reviews the diagnostic tests used to confirm the

diagnosis, including stool examination tests such as culture and sensitivity; the upper GI series; the use of sigmoidoscopy; and endoscopy. The endoscopic differences between ulcerative colitis and Crohn's disease are demonstrated. Dr. Kornbluth concludes with a discussion of the drug treatments available and the indications for each, including opiates and their derivatives, absorbants, anticholinergic agents, agents for treating inflammatory bowel disease (IBD), and octreotide. The video program confers CME credit. (AA-M).

- **Managing Diarrhea and Fecal Incontinence**

  Source: Libertyville, IL: Hollister Incorporated. 1992. (videocassette).

  Contact: Available from Hollister Incorporated. 2000 Hollister Drive, Libertyville, IL 60048. (800) 323-4060. PRICE: Single copy free.

  Summary: This videotape program guides nurses in managing diarrhea and fecal incontinence. The program features comments from various physicians and enterostomal therapy nurses. Topics include the time-consuming nature of dealing with fecal incontinence, psychosocial factors, fecal incontinence in institutionalized patients, the etiology of fecal incontinence and diarrhea, patient assessment, the nursing role, and the drawbacks of three treatment methods currently in use (diapers, absorbent pads, and rectal tubes). The program then introduces a new product from Hollister, the drainable fecal incontinence collector, and describes its advantages.

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 "diarrhea" (or synonyms) into the "For these words:" box. The following is a typical result when searching for sound recordings on diarrhea:

- **AIDS Update**

  Contact: California Medical Association, Audio Digest Foundation, 1577 E Chevy Chase Dr, Glendale, CA, 91206, (213) 245-8505.

  Summary: This soundrecording contains the transcripts of talks given to update physicians on AIDS and the practice of gastroenterology. The first speaker, Dr. John Cello, discusses the equipment, supplies, and universal endoscopy precautions used at the University of California San Francisco School of Medicine. He then discusses esophageal complaints, hepatic parenchymal disease, biliary tract disease, AIDS-related **diarrhea,** and therapies for each. Dr. Friedman's talk concerns gastrointestinal (GI) tract manifestations of HIV disease. It covers **diarrhea** and its etiologic agents; dysphagia/odynophagia; jaundice, hepatomegaly, or abnormal liver function; and their causative agents. The last speaker, Dr. Steven Wexner, discusses anorectal involvement in HIV disease. He describes Kaposi's sarcoma rectal lesions; HSV-2; Herpes proctitis; lumbosacral radiculopathy syndrome; anal carcinoma; and perianal sepsis. The cassette is accompanied by pre- and post-tests.

Bibliography: Multimedia on Diarrhea

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 diarrhea (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 diarrhea:

- **A Patient with diarrhea and vomiting [videorecording]** Source: produced by HumRRO, Human Resources Research Organization and Video Software Associates; Year: 1985; Format: Videorecording; San Diego, CA.: Intelligent Images, c1985
- **Bacterial and parasitic causes of diarrhea [slide].** Year: 1985; Format: Slide; [Columbus, Ohio]: Center for Continuing Medical Education, the Ohio State University College of Medicine, [1985]
- **Chronic diarrhea in infants and children [videorecording]** Source: Department of Pediatrics, Emory University, School of Medicine; Year: 1980; Format: Videorecording; Atlanta: Emory Medical Television Network: [for loan or sale by A. W. Calhoun Medical Library], 1980
- **Classification & abnormal physiology of diarrhea [slide]** Source: American Gastroenterological Association, in cooperation with the National Library of Medicine, National Medical Audiovisual Center; Year: 1978; Format: Slide; Atlanta: The Center, 1978
- **Diagnostic approach to chronic diarrhea: further diagnostic steps [slide]** Source: American Gastroenterological Association, in cooperation with the National Library of Medicine, National Medical Audiovisual Center; Year: 1978; Format: Slide; Atlanta: The Center; [Washington: for sale by National Audiovisual Center], 1978
- **Diagnostic approach to chronic diarrhea: the initial encounter [slide]** Source: American Gastroenterological Association, in cooperation with the National Library of Medicine, National Medical Audiovisual Center; Year: 1978; Format: Slide; Atlanta: The Center; [Washington: for sale by National Audiovisual Center], 1978
- **Diarrhea [slide]: pathology of common intestinal lesions causing diarrhea** Source: Joan Mattson; Year: 1972; Format: Slide; East Lansing, Mich.: Mattson: [for loan by Michigan State University, East Lansing, College of Human Medicine], 1972
- **General diarrhea [videorecording]** Source: [produced by] Hahnemann Medical College & Hospital and World Video Corp; Year: 1981; Format: Videorecording; [S.l.]: Medcare Associates, c1981
- **Infectious diarrhea [videorecording]** Source: [presented by] CME Productions, Inc., in cooperation with the Infectious Disease Section, Yale University, School of Medicine; Year: 1981; Format: Videorecording; [S.l.]: CME Productions, c1981
- **Infectious diarrhea [videorecording]** Source: presented by the Department of Medicine, Emory University, School of Medicine; Year: 1985; Format: Videorecording; Atlanta, Ga.: The University, 1985
- **Intestinal fluid secretion [slide]: secretory diarrhea** Source: American Gastroenterological Association, in cooperation with the National Library of Medicine, National Medical Audiovisual Center; Year: 1978; Format: Slide; Atlanta: The Center, 1978

- **Intestinal function & diarrhea [slide]** Source: National Medical Audiovisual Center; Year: 9999; Format: Slide; Atlanta: The Center; [Washington: for sale by National Audiovisual Center], 1975-
- **Malabsorption and diarrhea [slide]** Source: American Gastroenterological Association, in cooperation with the National Library of Medicine, National Medical Audiovisual Center; Year: 1978; Format: Slide; Atlanta: The Center, 1978
- **Nonspecific diarrhea [slide]** Source: American Gastroenterological Association, in cooperation with the National Library of Medicine, National Medical Audiovisual Center; Year: 1978; Format: Slide; Atlanta: The Center, 1978
- **Osmotic diarrhea & carbohydrate intolerance [slide]** Source: American Gastroenterological Association, in cooperation with the National Library of Medicine, National Medical Audiovisual Center; Year: 1978; Format: Slide; Atlanta: The Center, 1978
- **Pathophysiology of diarrhea [motion picture]: an approach to therapy** Source: Eaton [Laboratories]; Year: 1973; Format: Motion picture; Norwich, N. Y.: Eaton: [for loan by Norwich-Eaton Pharmaceuticals, Film Library], 1973
- **Pathophysiology of diarrhea [slide]** Source: American Gastroenterological Association; Year: 1979; Format: Slide; [Thorofare, N. J.]: The Association; [Timonium, Md.: for sale by Milner-Fenwick], c1979
- **Pharmacology of the symptomatic treatment of diarrhea [slide]** Source: American Gastroenterological Association, in cooperation with the National Library of Medicine, National Medical Audiovisual Center; Year: 1978; Format: Slide; Atlanta: The Center, 1978
- **Special features of infectious diarrhea in infants [slide]** Source: American Gastroenterological Association, in cooperation with the National Library of Medicine, National Medical Audiovisual Center; Year: 1978; Format: Slide; Atlanta: The Center, 1978
- **Traveller's diarrhea, Campylobacter gastroenteritis and cholera in the U.S.A. [videorecording]** Source: presented by Department of Medicine, Emory University, School of Medicine; Year: 1982; Format: Videorecording; Atlanta, Ga.: Emory Medical Television Network, 1982

CHAPTER 9. PERIODICALS AND NEWS ON DIARRHEA

Overview

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

News Services and Press Releases

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

- **Genzyme diarrhea drug takes longer than antibiotic**
  Source: Reuters Industry Breifing
  Date: October 20, 2003
- **Probiotic curbs diarrhea in kids on antibiotics**
  Source: Reuters Health eLine
  Date: October 14, 2003

- **Fermented milk shown to prevent antibiotic-induced diarrhea in children**
  Source: Reuters Medical News
  Date: October 14, 2003
- **IL-8 polymorphism predisposes to enteroaggregative E. coli diarrhea**
  Source: Reuters Medical News
  Date: September 11, 2003
- **Diarrhea-related HUS often has long-term sequelae, Shiga toxin binder not useful**
  Source: Reuters Medical News
  Date: September 09, 2003
- **Calcium supplementation reduces E. coli-related diarrhea**
  Source: Reuters Medical News
  Date: August 29, 2003
- **Prevalence of HIV-related diarrhea remains high in post-HAART era**
  Source: Reuters Medical News
  Date: May 19, 2003
- **Exclusive breastfeeding reduces diarrhea in babies**
  Source: Reuters Health eLine
  Date: April 25, 2003
- **Breastfeeding campaign safely prevents diarrhea in developing countries**
  Source: Reuters Medical News
  Date: April 25, 2003
- **Severe, refractory C. difficile diarrhea may respond to corticosteroids**
  Source: Reuters Industry Breifing
  Date: April 09, 2003
- **Fecal lactoferrin predicts invasive bacterial infection in children with diarrhea**
  Source: Reuters Medical News
  Date: March 13, 2003
- **Traveller's diarrhea bug may help treat colon cancer**
  Source: Reuters Health eLine
  Date: February 10, 2003
- **CFTR protein inhibitor may enhance cystic fibrosis research, diarrhea treatment**
  Source: Reuters Medical News
  Date: December 17, 2002
- **Romark gets FDA okay for pediatric diarrhea drug**
  Source: Reuters Industry Breifing
  Date: December 02, 2002

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

Newsletters on Diarrhea

Find newsletters on diarrhea using the Combined Health Information Database (CHID). You will need to use the "Detailed Search" option. To access CHID, go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Limit your search to "Newsletter" and "diarrhea." 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." Type "diarrhea" (or synonyms) into the "For these words:" box. The following list was generated using the options described above:

- **Kidney Disease**

  Source: Sarcoidosis Networking. 8(3): 2. May-June 2000.

Contact: Available from Sarcoid Network Association. Sarcoidosis Networking, 13925 80th Street East, Puyallup, WA 98372-3614. Email: sarcoidosis_network@prodigy.net.

Summary: Sarcoidosis is a chronic, progressive systemic granulomatous (causing lesions) disease of unknown cause (etiology), involving almost any organ or tissue, including the skin, lungs, lymph nodes, liver, spleen, eyes, and small bones of the hands or feet. This brief article, from a newsletter for patients with sarcoidosis, reviews kidney disease, its types, diagnosis, and management. The article begins with a summary of the anatomy and function of the kidneys, which filter the blood (removing waste and excess body fluids), and maintain the balance of some essential nutrients helping to regulate blood pressure, red blood cells, and elements such as potassium and calcium. Without functioning kidneys, one cannot live without dialysis, the mechanical filtration of the blood. Kidneys fail for a variety of reasons, including trauma to the kidney, toxins, heart failure, obstruction (kidney stones), overuse of some medications, and diseases that invade the kidney, such as sarcoidosis. Diabetes and high blood pressure are the most common causes for loss of kidney function. Warning signs of kidney disease are high blood pressure (hypertension), blood or protein in the urine, creatinine level greater than 1.2 in women or 1.4 in men, more frequent urination (especially at night), difficult or painful urination, and puffy eyes or swelling of the hands or feet (especially in children). Loss of kidney function can produce symptoms including fatigue, weakness, nausea, vomiting, **diarrhea** or constipation, headaches, loss of appetite, increased edema (fluid retention), and fever or chills. Kidney failure is characterized as acute kidney failure, chronic kidney insufficiency, and chronic kidney failure. The need to put a person on dialysis depends upon the levels of creatinine and urea nitrogen in the blood and the evaluation of body parameters such as fluid status, and symptoms of toxicity. The author encourages readers to practice preventive measures which include drinking 8 to 10 glasses of water per day, preventing or treating diabetes and high blood pressure, avoiding tobacco, eating a well balanced diet, practicing good hygiene, treating wounds and infections, limiting exposure to heavy metals and toxic chemicals, and avoiding unnecessary over the counter drug use.

- **Bowel Management Medication**

  Source: Pull-Thru Network News. 2(3): 4-5. Spring 1993.

  Contact: Available from Greater New York Pull-Thru Network. c/o Scott and Karen Brownlow, 4 Woody Lane, West Port, CT 06880. (201) 221-7530.

  Summary: This newsletter article provides information for parents about using various bowel management medications in their children. The introduction discusses the problems with differentiating between medications; the variety of medications on the market; how the FDA approves drugs; long-term usage and possible side effects; and using generic products. The remainder of the article is divided into two sections: laxatives and antidiarrheals. The laxative section covers bulk-forming laxatives, hyperosmotic laxatives (saline), lubricants, stimulant (contact) laxatives, and stool softeners. The antidiarrheal sections discusses opiates, polycarbophil, loperamide hydrochloride, aluminum powder (hydrated), bismuth subsalicylate, attapulgite, kaolin, activated charcoal, lactobacillus, and pectin. For each agent discussed, the author provides the brand name of product(s) that include that agent. The article concludes with a list of books and the address and telephone number for the National Digestive Diseases Information Clearinghouse for obtaining additional information.

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 "diarrhea" (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 diarrhea:

- **Controlling Incontinence by Controlling Diarrhea: The Role of Diet**

  Source: Intestinal Fortitude. 6(3): 7-10. Winter 1995-1996.

  Contact: Available from Intestinal Disease Foundation. 1323 Forbes Avenue, Suite 200, Pittsburgh, PA 15219. (412) 261-5888.

  Summary: This article helps patients understand the role of diet in controlling fecal incontinence, notably by controlling diarrhea. Topics include diarrhea and nutritional deficiencies; the role of meal size and composition; preservatives, alcohol, and caffeine; dietary fat, dietary fiber, and adequate fluids; the special role of pectin; and meal time recommendations. For each topic, the author provides specific suggestions for readers to incorporate into their meal habits.

- **Controlling Diarrhea in Patients With Short Bowel Syndrome**

  Source: Lifeline Letter. p. 1, 5, 8. May-June 1995.

  Contact: Available from Oley Foundation, Inc. A-23 Hun Memorial, Albany Medical Center, Albany, NY 12208. (800) 776-6539 or (518) 262-5079.

  Summary: This article, from a newsletter for people living with home parenteral or enteral nutrition, addresses diarrhea control in patients with short bowel syndrome (SBS). The author reviews recent dietary management ideas found in the literature. Also included is information from the 1995 American Society for Parenteral and Enteral Nutrition (ASPEN) Clinical Congress. Topics include how SBS leads to diarrhea; dietary suggestions, including the use of small, frequent feedings, and recommendations for liquid intake; the controversy over fat intake; and medication alternatives. The author recommends careful monitoring of the diet, with close attention to the response of extra fluid output caused by individual problem foods. She concludes that the ultimate goal for dietary therapy is to decrease the frequency and volume of diarrhea while providing for the nutritional needs of the person. 1 table.

- **Urgent Diarrhea: A Gut Reaction**

  Source: Intestinal Fortitude. 6(1): 1-3, 15. Summer 1995.

  Contact: Available from Intestinal Disease Foundation. 1323 Forbes Avenue, Suite 200, Pittsburgh, PA 15219. (412) 261-5888.

  Summary: This newsletter article explores the problem of urgent diarrhea. Topics include the role of diet, including lactose intolerance and foods to avoid; beverages; eating behaviors; drug therapy; the gastrocolic reflex; the neurocolic reflex; the use of behavior modification to manage the problem of urgent diarrhea; and finding resources

for additional assistance with this problem. The author provides practical suggestions for managing everyday situations affected by diarrhea.

- **Toddler's Diarrhea**

  Source: Newsletter for People With Lactose Intolerance and Milk Allergy. p. 9-10. December-January 1995-1996.

  Contact: Available from Newsletter for People With Lactose Intolerance and Milk Allergy. P.O. Box 3129, Ann Arbor, MI 48106-3129. (313) 572-9134.

  Summary: This newsletter article presents information about toddlers' diarrhea, a common type of chronic diarrhea in children. Topics include how toddlers' diarrhea differs from other forms of diarrhea, the need for continued fluids or oral rehydration therapy, possible contributing factors, the role of food allergy in diarrhea, and problems with diarrhea in day care centers. The author provides parents with specific suggestions for managing and preventing toddlers' diarrhea.

Academic Periodicals covering Diarrhea

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to diarrhea. In addition to these sources, you can search for articles covering diarrhea 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 diarrhea. One such source is the United States Pharmacopeia. In 1820, eleven physicians met in Washington, D.C. to establish the first compendium of standard drugs for the United States. They called this compendium the U.S. Pharmacopeia (USP). Today, the USP is a non-profit organization consisting of 800 volunteer scientists, eleven elected officials, and 400 representatives of state associations and colleges of medicine and pharmacy. The USP is located in Rockville, Maryland, and its home page is located at **http://www.usp.org/**. The USP currently provides standards for over 3,700 medications. The resulting USP DI® Advice for the Patient® can be accessed through the National Library of Medicine of the National Institutes of Health. The database is partially derived from lists of federally approved medications in the Food and Drug Administration's (FDA) Drug Approvals database, located at **http://www.fda.gov/cder/da/da.htm**.

While the FDA database is rather large and difficult to navigate, the Phamacopeia is both user-friendly and free to use. It covers more than 9,000 prescription and over-the-counter medications. To access this database, simply type the following hyperlink into your Web browser: **http://www.nlm.nih.gov/medlineplus/druginformation.html**. To view examples of a given medication (brand names, category, description, preparation, proper use, precautions, side effects, etc.), simply follow the hyperlinks indicated within the United States Pharmacopeia (USP).

Below, we have compiled a list of medications associated with diarrhea. 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 diarrhea:

Allopurinol

- **Systemic - U.S. Brands:** Aloprim; Zyloprim
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202021.html

Alosetron

- **Systemic - U.S. Brands:** Lotronex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500107.html

Anastrozole

- **Systemic - U.S. Brands:** Arimidex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203659.html

Anticholinergics/Antispasmodics

- **Systemic - U.S. Brands:** Anaspaz; A-Spas S/L; Banthine; Bentyl; Cantil; Cystospaz; Cystospaz-M; Donnamar; ED-SPAZ; Gastrosed; Homapin; Levbid; Levsin; Levsin/SL; Levsinex Timecaps; Pro-Banthine; Quarzan; Robinul; Robinul Forte; Symax SL; Transderm-Scop
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202049.html

Antidiabetic Agents, Sulfonylurea

- **Systemic - U.S. Brands:** Amaryl; DiaBeta; Diabinese; Dymelor; Glucotrol; Glucotrol XL; Glynase PresTab; Micronase; Orinase; Tolinase
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202742.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

Ascorbic Acid (Vitamin C)

- **Systemic - U.S. Brands:** Ascorbicap; Cecon; Cee-500; Cemill; Cenolate; Cetane; Cevi-Bid; Flavorcee; Ortho/CS; Sunkist
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202071.html

Attapulgite

- **Oral - U.S. Brands:** Diar-Aid; Diarrest; Diasorb; Diatrol; Donnagel; Kaopectate; Kaopek; K-Pek; Parepectolin; Rheaban
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202076.html

Beta-Carotene

- **Systemic - U.S. Brands:** Lumitene; Max-Caro
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202623.html

Bismuth Subsalicylate

- **Oral - U.S. Brands:** Bismatrol; Pepto-Bismol
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202092.html

Carbohydrates and Electrolytes

- **Systemic - U.S. Brands:** Infalyte; Kao Lectrolyte; Naturalyte; Oralyte; Pedialyte; Pedialyte Freezer Pops; Rehydralyte; Resol$
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202112.html

Charcoal, Activated

- **Oral - U.S. Brands:** Actidose with Sorbitol; Actidose-Aqua; CharcoAid; CharcoAid 2000; CharcoAid G; Insta-Char in an Aqueous Base; Insta-Char in an Aqueous Base with Cherry Flavor; Insta-Char Pediatric in an Aqueous Base with Cherry Flavor; Insta-Char Pediatric with Cherry
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202120.html

Cholestyramine

- **Oral - U.S. Brands:** Questran
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202137.html

Colestipol

- **Oral - U.S. Brands:** Colestid
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202161.html

Copper Supplements

- **Systemic - U.S. Brands:** Note:
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202164.html

Cromolyn

- **Oral - U.S. Brands:** Gastrocrom
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202169.html

Difenoxin and Atropine

- **Systemic - U.S. Brands:** Motofen
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202193.html

Diphenoxylate and Atropine

- **Systemic - U.S. Brands:** Lofene; Logen; Lomocot; Lomotil; Lonox; Vi-Atro
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202200.html

Diuretics, Loop

- **Systemic - U.S. Brands:** Bumex; Edecrin; Lasix; Myrosemide
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202205.html

Folic Acid (Vitamin B 9)

- **Systemic - U.S. Brands:** Folvite
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202250.html

Furazolidone

- **Oral - U.S. Brands:** Furoxone
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202252.html

Hydroxyurea

- **Systemic - U.S. Brands:** Droxia; Hydrea
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202291.html

Insulin

- **Systemic - U.S. Brands:** Humulin 50/50; Humulin 70/30; Humulin 70/30 Pen; Humulin L; Humulin N; Humulin N Pen; Humulin R; Humulin R, Regular U-500 (Concentrated); Humulin U; Lente; Lente Iletin II; Novolin 70/30; Novolin 70/30 PenFill; Novolin 70/30 Prefilled; Novolin L; Novoli
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203298.html

Ivermectin

- **Systemic - U.S. Brands:** Stromectol
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202311.html

Kaolin and Pectin

- **Oral - U.S. Brands:** Kao-Spen; Kapectolin; K-P
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202313.html

Laxatives

- **Oral - U.S. Brands:** Afko-Lube; Afko-Lube Lax 40; Agoral Marshmallow; Agoral Raspberry; Alaxin; Alophen; Alphamul; Alramucil Orange; Alramucil Regular; Bilagog; Bilax; Bisac-Evac; Black-Draught; Black-Draught Lax-Senna; Carter's Little Pills; Cholac; Chronulac; Cillium; Cit
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202319.html

Loperamide

- **Oral - U.S. Brands:** Imodium
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202332.html

Magnesium Supplements

- **Systemic - U.S. Brands:** Almora; Chloromag; Citroma; Concentrated Phillips' Milk of Magnesia; Mag-200; Mag-L-100; Magonate; Mag-Ox 400; Mag-Tab SR; Magtrate; Maox; MGP; Phillips' Chewable Tablets; Phillips' Milk of Magnesia; Slow-Mag; Uro-Mag
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202644.html

Metformin

- **Systemic - U.S. Brands:** Glucophage
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202756.html

Metronidazole

- **Systemic - U.S. Brands:** Flagyl; Protostat
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202365.html

Misoprostol

- **Systemic - U.S. Brands:** Cytotec
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202375.html

Narcotic Analgesics for Pain Relief

- **Systemic - U.S. Brands:** Astramorph PF; Buprenex; Cotanal-65; Darvon; Darvon-N; Demerol; Dilaudid; Dilaudid-5; Dilaudid-HP; Dolophine; Duramorph; Hydrostat IR; Kadian; Levo-Dromoran; M S Contin; Methadose; MS/L; MS/L Concentrate; MS/S; MSIR; Nubain; Numorphan; OMS Concentrate;
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202390.html

Niacin (Vitamin B 3)

- **Systemic - U.S. Brands:** Endur-Acin; Nia-Bid; Niac; Niacels; Niacor; Nico-400; Nicobid Tempules; Nicolar; Nicotinex Elixir; Slo-Niacin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202405.html

Niacin for High Cholesterol

- **Systemic - U.S. Brands:** Endur-Acin; Nia-Bid; Niac; Niacels; Niacor; Nico-400; Nicolar; Slo-Niacin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202404.html

Octreotide

- **Systemic - U.S. Brands:** Sandostatin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202421.html

Penicillins and Beta-Lactamase Inhibitors

- **Systemic - U.S. Brands:** Augmentin; Timentin; Unasyn; Zosyn
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202705.html

Polyethylene Glycol and Electrolytes

- **Local - U.S. Brands:** Co-Lav; Colovage; Colyte; Colyte-flavored; Go-Evac; GoLYTELY; NuLYTELY; OCL
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202636.html

Potassium Iodide

- **Systemic - U.S. Brands:** Pima
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202472.html

Pyridoxine (Vitamin B 6)

- **Systemic - U.S. Brands:** Beesix; Doxine; Nestrex; Pyri; Rodex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202493.html

Sulfonamides and Trimethoprim

- **Systemic - U.S. Brands:** Bactrim; Bactrim DS; Bactrim I.V.; Bactrim Pediatric; Cofatrim Forte; Cotrim; Cotrim DS; Cotrim Pediatric; Septra; Septra DS; Septra Grape Suspension; Septra I.V.; Septra Suspension; Sulfatrim; Sulfatrim Pediatric; Sulfatrim S/S; Sulfatrim Suspension; S
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202781.html

Thiamine (Vitamin B 1)

- **Systemic - U.S. Brands:** Biamine
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202560.html

Vancomycin

- **Oral - U.S. Brands:** Vancocin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202589.html

Commercial Databases

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. Or, you may be able to access these sources from your local medical library.

Mosby's Drug Consult™

Mosby's Drug Consult™ database (also available on CD-ROM and book format) covers 45,000 drug products including generics and international brands. It provides prescribing information, drug interactions, and patient information. Subscription information is available at the following hyperlink: **http://www.mosbysdrugconsult.com/**.

PDR*health*

The PDR*health* database is a free-to-use, drug information search engine that has been written for the public in layman's terms. It contains FDA-approved drug information adapted from the Physicians' Desk Reference (PDR) database. PDR*health* can be searched by brand name, generic name, or indication. It features multiple drug interactions reports. Search PDR*health* at **http://www.pdrhealth.com/drug_info/index.html**.

Other Web Sites

Drugs.com (**www.drugs.com**) reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. (**http://www.medletter.com/**) which allows users to download articles on various drugs and therapeutics for a nominal fee.

Researching Orphan Drugs

Although the list of orphan drugs is revised on a daily basis, you can quickly research orphan drugs that might be applicable to diarrhea by using the database managed by the National Organization for Rare Disorders, Inc. (NORD), at **http://www.rarediseases.org/**. Scroll down the page, and on the left toolbar, click on "Orphan Drug Designation Database." On this page (**http://www.rarediseases.org/search/noddsearch.html**), type "diarrhea" (or synonyms) into the search box, and click "Submit Query." When you receive your results, note that not all of the drugs may be relevant, as some may have been withdrawn from

orphan status. Write down or print out the name of each drug and the relevant contact information. From there, visit the Pharmacopeia Web site and type the name of each orphan drug into the search box at **http://www.nlm.nih.gov/medlineplus/druginformation.html**. You may need to contact the sponsor or NORD for further information.

NORD conducts "early access programs for investigational new drugs (IND) under the Food and Drug Administration's (FDA's) approval 'Treatment INDs' programs which allow for a limited number of individuals to receive investigational drugs before FDA marketing approval." If the orphan product about which you are seeking information is approved for marketing, information on side effects can be found on the product's label. If the product is not approved, you may need to contact the sponsor.

The following is a list of orphan drugs currently listed in the NORD Orphan Drug Designation Database for diarrhea:

- **Lactobin (trade name: Lactobin)**
  http://www.rarediseases.org/nord/search/nodd_full?code=207
- **human gammaglobulin**
  http://www.rarediseases.org/nord/search/nodd_full?code=1303
- **Cryptosporidium hyperimmune bovine colostrum IgG c**
  http://www.rarediseases.org/nord/search/nodd_full?code=359
- **Bovine colostrum**
  http://www.rarediseases.org/nord/search/nodd_full?code=634
- **Octreotide (trade name: Sandostatin LAR)**
  http://www.rarediseases.org/nord/search/nodd_full?code=935
- **Octreotride (trade name: Sandostatin LAR)**
  http://www.rarediseases.org/nord/search/nodd_full?code=936
- **Ocreotide (trade name: Sandostatin LAR)**
  http://www.rarediseases.org/nord/search/nodd_full?code=957

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[13]:

- 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/**

[13] 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.[14] 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:[15]

- **Bioethics:** Access to published literature on the ethical, legal, and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to cancer-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**

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[14] 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**).

[15] 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 "diarrhea" using the "Detailed Search" option. Go directly 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 "diarrhea" (or synonyms) into the "For these words:" box. The following is a sample result:

- **Diarrhea in the HIV/AIDS Patient**

  Contact: Medical Education Collaborative, 1800 Jackson St Ste 200, Golden, CO, 80401, (800) 442-6632, http://cmegateway.com.

  Summary: This guideline informs health professionals about human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS)-related diarrhea. The guideline provides the readers with an etiology of HIV-related diarrhea, and describes the various pathogens that may cause this ailment. It examines the use of antiretroviral drugs such as indinavir, nelfinavir, ritonavir, and saquinavir and their relation to the incidence rates of diarrhea in HIV-positive persons. The guideline makes recommendations for the treatment of diarrhea in HIV-positive persons. It provides a self-assessment quiz for health professionals to measure their knowledge of diarrhea in HIV/AIDS patients.

- **Treatment Strategies for OI's and Symptoms: Diarrhea in HIV Infection - Possible Causes, Diagnostic Techniques, and Therapies**

  Contact: Carl Vogel Center, 1012 14th St NW Ste 707, Washington, DC, 20005, (202) 638-0750.

  Summary: This paper discusses treatment strategies for opportunistic infections, more specifically diarrhea, in HIV infection. It also explores possible causes, diagnostic techniques, and therapies. Diarrhea in people living with HIV can have many causes, and ranges in severity. Studies show that examination of diarrhea can lead to the identification of disease-causing organisms. The most severe diarrhea is normally caused by cryptosporidiosis, instigated by a protozoal infection. Isosporiasis, microsporidiosis, cytomegalovirus colitis, and bacterial infections also cause diarrhea. Diarrhea can also be caused by food allergy reactions. The paper goes on to discuss how to diagnose and analyze stool. It talks about parasites including parvum. A number of prescription drugs used for the treatment of diarrhea are described. Candida and parasites are often believed to be present in Persons With AIDS (PWA's) and may cause problems if they remain unrecognized. Mycobacterium Avium Complex (MAC) can cause bodywide infection, but the most common lasting symptom is a chronic, wasting diarrhea.

The NLM Gateway[16]

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.[17] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "diarrhea" (or synonyms) into the search box and click "Search." The results will be presented in a tabular form, indicating the number of references in each database category.

Results Summary

Category	Items Found
Journal Articles	59658
Books / Periodicals / Audio Visual	2592
Consumer Health	1037
Meeting Abstracts	1102
Other Collections	2
Total	64391

HSTAT[18]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[19] 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.[20] Simply search by "diarrhea" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

Coffee Break: Tutorials for Biologists[21]

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

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

[17] 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).

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

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

[20] 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.

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

staff.[22] 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.[23] This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

The Genome Project and Diarrhea

In the following section, we will discuss databases and references which relate to the Genome Project and diarrhea.

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).[24] 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 "diarrhea" (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 diarrhea:

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[22] 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.

[23] 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.

[24] 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.

- **Chloride Diarrhea, Familial**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?214700
- **Diarrhea, Chronic, with Villous Atrophy**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?520100
- **Diarrhea, Fatal Infantile, with Abnormal Hair**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?222470
- **Diarrhea, Glucose-stimulated Secretory, with Common Variable Immunodeficiency**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?125890
- **Secretory Diarrhea, Myopathy, and Deafness**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?607540
- **Sodium Diarrhea, Congenital**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?270420

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 site categorizes each disorder by system 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 "diarrhea" (or synonyms) into the search box and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[25]

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 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[26]

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 "diarrhea" (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).

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[25] Adapted from the National Library of Medicine:
http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html.

[26] 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 diarrhea 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 diarrhea. 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 diarrhea. 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 "diarrhea":

- Other guides

  Digestive Diseases
  http://www.nlm.nih.gov/medlineplus/digestivediseases.html

  Food Contamination/Poisoning
  http://www.nlm.nih.gov/medlineplus/foodcontaminationpoisoning.html

  Gastroenteritis
  http://www.nlm.nih.gov/medlineplus/gastroenteritis.html

  Giardia Infections
  http://www.nlm.nih.gov/medlineplus/giardiainfections.html

  Irritable Bowel Syndrome
  http://www.nlm.nih.gov/medlineplus/irritablebowelsyndrome.html

  Nausea and Vomiting
  http://www.nlm.nih.gov/medlineplus/nauseaandvomiting.html

  Rotavirus Infections
  http://www.nlm.nih.gov/medlineplus/rotavirusinfections.html

Within the health topic page dedicated to diarrhea, the following was listed:

- General/Overviews

  Diarrhea
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=DS00292

- Diagnosis/Symptoms

  Abdominal Pain, Acute: Self-Care Flowcharts
  Source: American Academy of Family Physicians
  http://familydoctor.org/flowcharts/527.html

  Abdominal Pain, Chronic: Self-Care Flowcharts
  Source: American Academy of Family Physicians
  http://familydoctor.org/flowcharts/528.html

  Colonoscopy
  http://www.nlm.nih.gov/medlineplus/tutorials/colonoscopyloader.html

  Colonoscopy
  Source: National Digestive Diseases Information Clearinghouse
  http://digestive.niddk.nih.gov/ddiseases/pubs/colonoscopy/index.htm

  Diarrhea: Self-Care Flowcharts
  Source: American Academy of Family Physicians
  http://familydoctor.org/flowcharts/534.html

  Flexible Sigmoidoscopy
  Source: National Digestive Diseases Information Clearinghouse
  http://digestive.niddk.nih.gov/ddiseases/pubs/sigmoidoscopy/index.htm

Radiography-Lower GI Tract (Barium Enema "BE")
Source: American College of Radiology, Radiological Society of North America
http://www.radiologyinfo.org/content/lower_gi.htm

- Specific Conditions/Aspects

  Antibiotic-Associated Diarrhea
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=DS00454

  Chronic Diarrhea
  Source: National Center for Infectious Diseases, Division of Parasitic Diseases
  http://www.cdc.gov/ncidod/dpd/parasites/diarrhea/factsht_chronic_diarrhea.htm

  Preventing Dehydration From Diarrhea
  Source: American Medical Association
  http://www.medem.com/medlb/article_detaillb.cfm?article_ID=ZZZSDZ72AKC&sub_cat=195

  Travelers' Diarrhea: Frequently Asked Questions
  Source: Centers for Disease Control and Prevention
  http://www.cdc.gov/ncidod/dbmd/diseaseinfo/travelersdiarrhea_g.htm

- Children

  Are Your Bowels Moving?
  Source: Nemours Foundation
  http://kidshealth.org/kid/stay_healthy/body/bowel.html

  Elimination Problems in Infants and Children: Self-Care Flowcharts
  Source: American Academy of Family Physicians
  http://familydoctor.org/flowcharts/533.html

  Gastrointestinal Infections and Diarrhea
  Source: Nemours Foundation
  http://kidshealth.org/parent/medical/digestive/gastrointestinal.html

  Stool Tests
  Source: Nemours Foundation
  http://kidshealth.org/parent/general/sick/labtest8.html

  Treating Diarrhea and Dehydration
  Source: American Academy of Pediatrics
  http://www.medem.com/search/article_display.cfm?path=n:&mstr=/ZZZAHYUYQ7C.html&soc=AAP&srch_typ=NAV_SERCH

  Vomiting and Diarrhea: Helping Your Child through Sickness
  Source: American Academy of Family Physicians
  http://familydoctor.org/healthfacts/196/

- From the National Institutes of Health

  Diarrhea
  Source: National Digestive Diseases Information Clearinghouse
  http://digestive.niddk.nih.gov/ddiseases/pubs/diarrhea/index.htm

- Organizations

  American Gastroenterological Association
  http://www.gastro.org/

  National Institute of Allergy and Infectious Diseases
  http://www.niaid.nih.gov/

  National Institute of Diabetes and Digestive and Kidney Diseases
  http://www.niddk.nih.gov/

- Prevention/Screening

  Food and Water Precautions and Travelers' Diarrhea
  Source: National Center for Infectious Diseases
  http://www.cdc.gov/travel/foodwatr.htm

- Research

  Bacteria in Condiment Sauces on Tables in Mexican-Style Restaurants in Guadalajara, Mexico, and Houston, Texas
  Source: American College of Physicians
  http://www.annals.org/cgi/content/full/136/12/I-56

- Teenager

  Gastrointestinal Infections and Diarrhea
  Source: Nemours Foundation
  http://kidshealth.org/teen/infections/intestinal/diarrhea.html

You may also choose to use the search utility provided by MEDLINEplus at the following Web address: **http://www.nlm.nih.gov/medlineplus/**. Simply type a keyword into the search box and click "Search." This utility is similar to the NIH search utility, with the exception that it only includes materials that are linked within the MEDLINEplus system (mostly patient-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The Combined Health Information Database (CHID)

CHID Online is a reference tool that maintains a database directory of thousands of journal articles and patient education guidelines on diarrhea. 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:

- **Acute Diarrhea in Children**

  Source: Flourtown, PA: American Society for Pediatric Gastroenterology, Hepatology and Nutrition. 2003. 1 p.

  Contact: Available from North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). PO Box 6, Flourtown, PA 19031. (215) 233-

0808. Fax: (215) 233-3939. Website: www.naspgn.org. PRICE: Full-text available online at no charge; contact organization for print copies.

Summary: Acute diarrhea is one of the most common illnesses in children and a common reason for doctor visits. The most common causes of acute diarrhea are viruses, bacteria and parasites, food poisoning, medications (especially antibiotics), food allergies, enzyme deficiencies (as in lactose intolerance), and toxic substances. This brief fact sheet considers acute diarrhea (defined as lasting less than one week) in children. The fact sheet defines the condition, then discusses its incidence (how common it is), the causes of the condition, diagnostic tests used to identify and confirm the problem, and treatment options. Acute diarrhea stops when the body clears the infection or toxic causing the problem. Most viruses and bacteria do not require treatment with antibiotics. If the diarrhea persists for longer than one or two weeks, stool and blood tests will help determine the most likely cause of the problem and can guide treatment strategies. Children with acute diarrhea should continue to eat their regular diet, unless the diarrhea is severe or accompanied by vomiting. In that case, replacement fluid mineral drinks are recommended. For more information, readers are encouraged to visit www.naspghan.org (the web site of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition).

- **Dietary Suggestions for Managing Diarrhea**

  Source: Rochester, MN: Mayo Clinic, Patient and Health Education Center. 1990. 2 p.

  Contact: Available from Mayo Clinic, Patient and Health Education Center. 200 First Street , SW, Rochester, MN 55905. (507) 284-2511. PRICE: $0.80 plus shipping and handling (for health care professionals). Order Number MC590/R290.

  Summary: Diarrhea may be caused by some drugs, chemotherapy, radiation therapy, stress, intestinal surgery, or sensitivity to certain foods. This patient education brochure offers dietary suggestions for managing diarrhea. Topics include limiting foods that contain fiber; increasing the use of low-fiber foods; managing lactose intolerance; meal planning and scheduling; the importance of adequate fluid intake; and the use of a clear liquid diet to rest the bowel. The brochure includes blank spaces for the listing of health care providers and phone numbers.

- **Diarrhea and Dehydration: Guidelines for Patients**

  Source: Elk Grove Village, IL: American Academy of Pediatrics. 1996. 2 p.

  Contact: Available from American Academy of Pediatrics. P.O. Box 927, Elk Grove Village, IL 60009-0927. (800) 433-9016 or (847) 228-5005. Fax (847) 228-1281. PRICE: $29.95 for package of 100 brochures for members; $34.95 for nonmembers.

  Summary: This brochure outlines the treatment of diarrhea in children. Written to answer questions commonly asked by parents, the brochure covers the causes of diarrhea, when to contact the health care provider, how long the diarrhea can be expected to last, special fluids and diet for mild illness, moderate diarrhea and its treatment, diagnosing severe illness, the use of medications, and home remedies. The brochure concludes with a reminder of recommended care strategies. Most diarrhea in children is caused by one of several viruses and gets better by itself within a week. A health care provider should be contacted if the child with diarrhea is less than 6 months of age or if any of these symptoms are present: blood in stool, frequent vomiting, abdominal pain, less frequent than normal urination, no tears when crying, loss of appetite for liquids, high fever, frequent diarrhea, dry mouth, weight loss, or extreme

thirst. However, even if diarrhea is present, as long as the child acts well and is taking adequate fluids and food, loose stools are not a great concern. Parents are encouraged to help their children maintain food and fluid intake during periods of diarrhea. The brochure notes the availability of additional publications from the American Academy of Pediatrics.

- **Self-Care for Vomiting and Diarrhea**

  Source: San Bruno, CA: Krames Communications. 1995. 2 p.

  Contact: Available from Krames Communications. Order Department, 1100 Grundy Lane, San Bruno, CA 94066. (800) 333-3032. Fax (415) 244-4512. PRICE: $17.95 per pack of 50 brochures (as of 1996).

  Summary: This brochure provides basic suggestions for readers coping with vomiting and diarrhea. The brochure first describes the causative agents of stomach upset and then provides recommendations for relieving digestive discomfort. Suggestions include drinking liquids, starting with light meals, using stomach-soothing medications, and avoiding stomach-upsetting medications. The brochure includes two checklists: the symptoms of dehydration (excess fluid loss) and when to call a health care provider. The brochure is illustrated with colorful drawings.

- **What About Diarrhea?**

  Contact: AIDS Committee of Toronto, 399 Church St 4th Fl, Toronto, (416) 340-2437, http://www.actoronto.org.

  Summary: This brochure, in a question-and-answer format, advises HIV-positive people what happens to cause diarrhea and how to eat to avoid it.

- **Functional Diarrhea: Some Answers to Often Asked Questions**

  Source: Milwaukee, WI: International Foundation for Functional Gastrointestinal Disorders. 1994. 2 p.

  Contact: Available from International Foundation for Functional Gastrointestinal Disorders (IFFGD). P.O. Box 170864, Milwaukee, WI 53217. (888) 964-2001 or (414) 964-1799. Fax (414) 964-7176. E-mail: iffgd@iffgd.org. Website: www.iffgd.org. PRICE: $0.50.

  Summary: This fact sheet answers common questions about functional diarrhea. Diarrhea is defined as an abnormal looseness of stools and or an increase in frequency of bowel movements. On the basis of surveys of normal populations, more than three bowel movements per day may be defined as diarrhea. If diarrhea lasts longer than three weeks, it is classified as chronic. If no specific cause is found after a thorough investigation, and if certain criteria are met, a diagnosis of functional diarrhea may be considered. Patients with functional diarrhea may represent a subgroup of patients with irritable bowel syndrome (IBS). The most important aspect of the workup for the patient is a thorough medical history, including use of medicines and dietary habits, and a careful physical examination. Patients may have celiac disease (gluten intolerance) or lactose (milk sugar) intolerance as the underlying cause of their diarrhea. In these cases, dietary therapy is indicated. Although there is no consensus regarding the cause of functional diarrhea, it is thought that patients with functional diarrhea have different gastrointestinal motility (movement) patterns than do patients without diarrhea. Treatments often include an increase in dietary fiber. The fact sheet also briefly mentions drugs that can be used for a limited period to manage diarrheal episodes. (AA-M).

- **Diarrhea : Antidiarrheal Drugs**

  Contact: Project Inform, HIV Treatment Hotline, 205 13th St Ste 2001, San Francisco, CA, 94103, (415) 558-8669, http://www.projectinform.org.

  Summary: This fact sheet discusses diarrhea and the therapeutic drugs used in its treatment for persons with the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS). The fact sheet examines the various causes of diarrhea in persons with HIV/AIDS and the symptoms of these ailments. It provides information concerning the drugs that can be used in the treatment of diarrhea, thereby helping to prevent wasting syndrome. It explains the diagnostic process that can be used to determine the causes of diarrhea as well as the principles of treating a person with HIV/AIDS suffering from one of these conditions.

- **Diarrhea, Acute**

  Source: in Griffith, H.W. Instructions for Patients. 5th ed. Philadelphia, PA: W.B. Saunders Company. 1994. p. 124.

  Contact: Available from W.B. Saunders Company. Book Order Fulfillment, 6277 Sea Harbor Drive, Orlando, FL 32887-4430. (800) 545-2522. Fax (800) 874-6418. PRICE: $49.95. ISBN: 0721649300 (English); 0721669972 (Spanish).

  Summary: This fact sheet provides basic information on frequent signs and symptoms, causes, risk factors, preventive measures, etc.; treatment, medication, and diet; and when to contact one's health care provider. The fact sheet is designed to be photocopied and distributed to patients as a reinforcement of oral instructions and as a teaching tool. The book in which the fact sheet appears is available in English or Spanish.

- **Dietary Help for Controlling Diarrhea**

  Contact: AIDS Services of Austin, PO Box 4874, Austin, TX, 78765-9836, (512) 458-2437, http://www.asaustin.org.

  Summary: This fact sheet provides detailed recommendations for replacing or modifying the intake of lactose, fiber, and fat in the diet of persons experiencing diarrhea, one of the gastrointestinal diseases and disorders associated with Acquired immunodeficiency syndrome (AIDS), caused by Human immunodeficiency virus (HIV).

- **Diarrhea**

  Source: Bethesda, MD: National Digestive Diseases Information Clearinghouse (NDDIC), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health. 1999. 5 p.

  Contact: Available from National Digestive Diseases Information Clearinghouse (NDDIC). 2 Information Way, Bethesda, MD 20892-3570. (800) 891-5389 or (301) 654-3810. Fax (301) 634-0716. E-mail: nddic@info.niddk.nih.gov. Website: www.niddk.nih.gov. PRICE: Full-text available online at no charge; single copy free; bulk copies available. Order number: DD-185.

  Summary: This fact sheet provides information about the causes, treatment, and prevention of diarrhea, defined as loose, watery stools occurring more than three times in one day. Diarrhea can cause dehydration, which means the body lacks enough fluid to function properly. The fact sheet emphasizes that diarrhea is a common problem that usually resolves on its own. Diarrhea is dangerous if a person becomes dehydrated. Causes of diarrhea include viral, bacterial, or parasitic infections; food intolerance;

reactions to medicine; intestinal diseases; and functional bowel disorders. Treatment involves replacing lost fluids and electrolytes. Depending on the cause of the problem, a person might also need medication to stop the diarrhea or treat an infection. Children may need an oral rehydration solution to replace lost fluids and electrolytes. A health care provider should be consulted if a person with diarrhea has severe pain in the abdomen or rectum, a fever of 102 degrees Fahrenheit or higher, blood in the stool, signs of dehydration, or diarrhea for more than 3 days. One section of the fact sheet discusses strategies that can help to prevent traveler's diarrhea. The fact sheet includes a brief discussion of the activities of the National Digestive Diseases Information Clearinghouse, a federal service that provides information about digestive diseases to people with digestive disorders and to their families, health care professionals, and the public.

- **Treating Diarrhea and Constipation**

  Source: San Bruno, CA: Krames Communications. 1998. 2 p.

  Contact: Available from Krames Communications. 1100 Grundy Lane, San Bruno, CA 94066-3030. (800) 333-3032. Fax (415) 244-4512. PRICE: $12.50 for pad of 50 sheets.

  Summary: This fact sheet provides suggestions on treating diarrhea and constipation in patients receiving chemotherapy and radiation therapy. These side effects occur because the treatment affects normal cells as well as cancer cells. The fact sheet lists tips to control diarrhea: limit the amount of fiber and milk in the diet; eat foods rich in potassium (bananas and oranges); eat small, frequent meals; drink plenty of fluids; and avoid coffee, tea and alcohol. The fact sheet notes that diarrhea may also be helped with medication. Advise on when to contact a health care provider is given as are the following strategies to avoid constipation: eat high-fiber foods, drink plenty of fluids, and exercise often. The fact sheet is illustrated with full-color line drawings and includes blank space for notes or special instructions. The fact sheet is one of a series of patient education materials on the complications of cancer treatment.

- **Antidiarrheal Therapy**

  Source: Canadian Journal of Gastroenterology. 13(3): 207-208. April 1999.

  Contact: Available from Pulsus Group, Inc. 2902 South Sheridan Way, Oakville, Ontario, Canada L6J 7L6.

  Summary: This fact sheet, from a professional journal of gastroenterology, guides patients who have been advised to use an antidiarrheal medication. The fact sheet describes various medications used to control diarrhea and the potential risks involved in taking these drugs. Diarrhea is defined as more water in the stool than normal. Antidiarrheal medications are helpful for occasional or short term treatment of diarrhea that the physician does not feel is specifically caused by an inflammatory or serious infectious disease of the intestines. Patients with irritable bowel syndrome (IBS) occasionally take these medications to control diarrhea. The most commonly used antidiarrheal medications are loperamide hydrochloride (Apo Loperamide or Imodium), diphenoxylate with atropine (Lomotil), codeine, bismuth subsalicylate (Pepto Bismol), and cholestyramine (Questran). Most of these medications (all except cholestyramine) work by slowing the movement of food through the intestines. This gives the intestine more time to absorb the water and makes the stool less watery. Cholestyramine binds to the bile in the intestines, helping certain patients (particularly those who have had surgery to remove a section of their small intestine) have fewer problems with diarrhea. These medications are generally very safe for patients with

mild diarrhea but can be potentially dangerous for patients with severe diarrhea. Patients are encouraged to work closely with their physicians to manage any problems.

- **Epidemiology of Three Diarrheal Diseases**

  Source: Arlington, VA: American College of Gastroenterology. 1993. 2 p.

  Contact: Available from American College of Gastroenterology. 4900B South 3rd Street, Arlington, VA 22206-1656. (703) 820-7400. PRICE: Single copy free.

  Summary: This fact sheet, written for physicians in gastroenterologic practice as well as for primary care physicians, summarizes the epidemiology of three diarrheal diseases. Diseases include Salmonella enteritidis infections; Brainerd diarrhea; and Escherichia coli 0157: H7 infections. For each condition, the author provides a brief review of current knowledge, epidemiology, and diagnostic suggestions. 4 references.

- **Diarrhea: Steps to Recovery**

  Source: San Bruno, CA: StayWell Company. 1999. [2 p.].

  Contact: Available from StayWell Company. Order Department, 1100 Grundy Lane, San Bruno, CA 94066-9821. (800) 333-3032. Fax (650) 244-4512. E-mail: email@staywell.com. Website: www.staywell.com. PRICE: $17.95 for pack of 50; plus shipping and handling.

  Summary: This patient education brochure describes diarrhea and its treatment. Written in nontechnical language, the brochure first defines diarrhea as bowel movements that occur more frequently or are more watery than usual. Symptoms of diarrhea include looser, more watery stools than normal, more frequent stools than normal, more urgent need to pass stool, and pain or spasms in the digestive tract. Things that may irritate the digestive tract and lead to diarrhea include harmful bacteria or viruses or medications. Certain foods can cause diarrhea in some people; stress and anxiety can lead to diarrhea in others. Diagnosis will include the patient's medical history and some diagnostic tests such as stool sample testing and sigmoidoscopy. Treatment of the diarrhea depends on its cause. Diarrhea caused by infection needs to be treated by eradicating the underlying infection. Other treatment options can include an increase in drinking fluids, prescription medications, fasting, and following the BRAT (bananas, rice, applesauce, toast) diet. The brochure reminds readers to contact their health care provider if they have severe pain, high fever or bloody stool, or symptoms of dehydration. One section of the brochure illustrates and describes the physiology of normal bowel movements and what happens in diarrhea. The last page of the brochure summarizes the recommendations for recovering from diarrhea. The brochure is illustrated with full color line drawings. 6 figures.

- **Vomiting and Diarrhea: Helping Your Child Through Sickness**

  Source: Kansas City, MO: American Academy of Family Physicians. 1993. 4 p.

  Contact: Available from American Academy of Family Physicians. 11400 Tomahawk Creek Parkway, Leawood, KS 66211-2672. (800) 274-2237. Website: www.aafp.org. PRICE: $22.00 for 100 copies for members, $33.00 for 100 copies for nonmembers.

  Summary: This patient education brochure helps parents understand vomiting and diarrhea and how they can help their child through sickness. Vomiting (throwing up) and diarrhea (frequent, watery bowel movements) can be caused by viruses, bacteria, parasites, foods that are hard to digest, and other things. Vomiting and diarrhea can be harmful to children because they can cause dehydration. Fluids can be replaced by oral

rehydration solutions (ORS). The brochure explains the different types of ORS, including powders and premixed liquids, and home remedies. The brochure also outlines how much ORS to give to a child with diarrhea or with vomiting. The brochure also recommends feeding a child during illness. Even though eating may cause the amount of diarrhea to increase, the child will be able to get some nutrients from the food. This may prevent too much weight loss and may enable the child to get better more quickly. The brochure notes that medications to stop diarrhea are not usually needed. A final section outlines diarrhea prevention strategies, focusing on handwashing and hygienic considerations. One sidebar lists the signs of dehydration in children and babies. 2 tables. (AA-M).

- **All About Travellers' Diarrhea**

  Source: London, England: British Digestive Foundation. 1993. 3 p.

  Contact: Available from British Digestive Foundation. 7 Chandos Street, London W1A 2LN England. PRICE: Single copy free.

  Summary: This patient education brochure provides basic information about traveller's diarrhea. Written in a question-and-answer format, it addresses symptoms; steps to prevent traveller's diarrhea; what to do if an attack strikes; and how to know when to consult a health care provider. The brochure includes an insert summarizing guidelines for the early diagnosis of digestive disorders. This insert, entitled 'When Should I See My Doctor' lists symptoms that suggest a health care provider should be consulted. The brochure concludes with a brief description of the activities of the British Digestive Foundation.

- **Vomiting and Diarrhea in Children**

  Source: American Family Physician. 51(5): 1117-1118. April 1995.

  Summary: This patient information fact sheet about vomiting and diarrhea in children, from the American Family Physician journal, is designed for reproduction and distribution to parents. Written in a question and answer format, the fact sheet covers the risk of getting dehydrated; how to prevent dehydration; oral rehydration solution (ORS); home remedies for dehydration; how ORS should be given; how long to give ORS; breast feeding and formula feeding for the child with diarrhea; medications for diarrhea; and how to determine if a dehydrated child needs to be hospitalized.

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search this site located at **http://www.guideline.gov/** by using the keyword "diarrhea" (or synonyms). The following was recently posted:

- **American Gastroenterological Association medical position statement: guidelines for the evaluation and management of chronic diarrhea**

  Source: American Gastroenterological Association - Medical Specialty Society; 1998 November 8 (reviewed 2001); 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3065&nbr=2291&string=diarrhea

- **American Gastroenterological Association medical position statement: guidelines for the management of malnutrition and cachexia, chronic diarrhea, and hepatobiliary disease in patients with human immunodeficiency virus infection**

  Source: American Gastroenterological Association - Medical Specialty Society; 1996 December (reviewed 2001); 31 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=837&nbr=41&string=diarrhea

- **Practice guidelines for the management of infectious diarrhea**

  Source: Infectious Diseases Society of America - Medical Specialty Society; 2001 February; 21 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2791&nbr=2017&string=diarrhea

Healthfinder™

Healthfinder™ is sponsored by the U.S. Department of Health and Human Services and offers links to hundreds of other sites that contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines. The following was recently found in this database:

- **Brainerd Diarrhea**

  Summary: This online mini fact sheet provides basic information on brainerd diarrhea, a gastrointestinal disorder. The fact sheet includes information about symptoms, diagnosis and treatment.

  Source: National Center for Infectious Diseases, Centers for Disease Control and Prevention

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=2086

- **Campylobacter**

  Summary: This document provides answers to consumers' questions about Campylobacter -- the most common bacterial cause of diarrheal illness in the United States.

  Source: National Center for Infectious Diseases, Centers for Disease Control and Prevention

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=3880

- **Childhood Diarrhea: Messages for Parents**

  Summary: This consumer health information brochure describes diarrhea symptoms, causes, spread and treatment and prevention.

  Source: Centers for Disease Control and Prevention, U.S. Department of Health and Human Services

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=5070

- **Irritable Bowel Syndrome in Children**

  Summary: Irritable bowel syndrome (IBS) is a digestive disorder that causes abdominal pain, bloating, gas, diarrhea, and constipation--or some combination of these problems.

  Source: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6514

- **Lotronex Information**

  Summary: This page presents information for women using the prescription drug Lotronex (alosetron hydrochloride) for treatment of the diarrhea-predominant form of irritable bowel syndrome (IBS).

  Source: Center for Drug Evaluation and Research, U.S. Food and Drug Administration

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=5504

- **Sigmoidoscopy**

  Summary: Basic information about sigmoidoscopy -- a medical procedure that allows a physician to look at the inside of the large intestine to determine the cause of diarrhea, abdominal pain and constipation,

  Source: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=4977

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 diarrhea. The drawbacks of this approach are that the information is not organized by theme and that the references are often a mix of information for professionals and patients. Nevertheless, a large number of the listed Web sites provide useful background information. We can only recommend this route, therefore, for relatively rare or specific disorders, or when using highly targeted searches. To use the NIH search utility, visit the following Web page: **http://search.nih.gov/index.html**.

Additional Web Sources

A number of Web sites are available to the public that often link to government sites. These can also point you in the direction of essential information. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=168&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/specific.htm**
- Google: **http://directory.google.com/Top/Health/Conditions_and_Diseases/**

- Med Help International: **http://www.medhelp.org/HealthTopics/A.html**
- Open Directory Project: **http://dmoz.org/Health/Conditions_and_Diseases/**
- Yahoo.com: **http://dir.yahoo.com/Health/Diseases_and_Conditions/**
- WebMD®Health: **http://my.webmd.com/health_topics**

Finding Associations

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

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 diarrhea. 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 "diarrhea" (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 "diarrhea". 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 "diarrhea" (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 "diarrhea" (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.[27]

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

[27] 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)[28]:

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute)
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System, Humboldt), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos, **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**
- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** Los Gatos PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation, Sacramento), **http://suttermedicalcenter.org/library/**
- **California:** Health Sciences Libraries (University of California, Davis), **http://www.lib.ucdavis.edu/healthsci/**
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System, Pleasanton), **http://gaelnet.stmarys-ca.edu/other.libs/gbal/east/vchl.html**
- **California:** Washington Community Health Resource Library (Fremont), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.saintjosephdenver.org/yourhealth/libraries/**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**

[28] 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 diarrhea:

- **Basic Guidelines for Diarrhea**

  Diarrhea
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003126.htm

- **Signs & Symptoms for Diarrhea**

  Abdominal pain
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003120.htm

  Blood in the stool
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003130.htm

  Confusion
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003205.htm

  Dry skin
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003250.htm

Fever
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003090.htm

Gastrointestinal bleeding
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003133.htm

Nausea
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

Pain while passing stool
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003131.htm

Rapid heart rate
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003077.htm

Skin turgor
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003281.htm

Stools - floating
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003128.htm

Tenesmus
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003131.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

- **Diagnostics and Tests for Diarrhea**

BUN
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003474.htm

Chem-20
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003468.htm

Creatinine
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003475.htm

IgA
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003544.htm

Urine specific gravity
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003587.htm

- **Nutrition for Diarrhea**

Bulk
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002470.htm

Coffee
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002445.htm

Fats
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002468.htm

Fiber
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002470.htm

Protein
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002467.htm

Yogurt
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002463.htm

- **Background Topics for Diarrhea**

Chemotherapy
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002324.htm

Electrolyte
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002350.htm

Electrolytes
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002350.htm

Enterotoxin
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002352.htm

Gastrectomy
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002945.htm

Physical examination
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002274.htm

Radiation therapy
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001918.htm

Systemic
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002294.htm

Toxins
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002331.htm

Online Dictionary Directories

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): **http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical**

- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): **http://mel.lib.mi.us/health/health-dictionaries.html**
- Patient Education: Glossaries (DMOZ Open Directory Project): **http://dmoz.org/Health/Education/Patient_Education/Glossaries/**
- Web of Online Dictionaries (Bucknell University): **http://www.yourdictionary.com/diction5.html#medicine**

DIARRHEA 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]

Ablation: The removal of an organ by surgery. [NIH]

Abrasion: 1. The wearing away of a substance or structure (such as the skin or the teeth) through some unusual or abnormal mechanical process. 2. An area of body surface denuded of skin or mucous membrane by some unusual or abnormal mechanical process. [EU]

Abscess: Accumulation of purulent material in tissues, organs, or circumscribed spaces, usually associated with signs of infection. [NIH]

Acceptor: A substance which, while normally not oxidized by oxygen or reduced by hydrogen, can be oxidized or reduced in presence of a substance which is itself undergoing oxidation or reduction. [NIH]

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

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]

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

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

Acquired Immunodeficiency Syndrome: An acquired defect of cellular immunity associated with infection by the human immunodeficiency virus (HIV), a CD4-positive T-lymphocyte count under 200 cells/microliter or less than 14% of total lymphocytes, and increased susceptibility to opportunistic infections and malignant neoplasms. Clinical manifestations also include emaciation (wasting) and dementia. These elements reflect criteria for AIDS as defined by the CDC in 1993. [NIH]

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

Action Potentials: The electric response of a nerve or muscle to its stimulation. [NIH]

Acuity: Clarity or clearness, especially of the vision. [EU]

Acute renal: A condition in which the kidneys suddenly stop working. In most cases, kidneys can recover from almost complete loss of function. [NIH]

Acyl: Chemical signal used by bacteria to communicate. [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]

Adenosine Diphosphate: Adenosine 5'-(trihydrogen diphosphate). An adenine nucleotide containing two phosphate groups esterified to the sugar moiety at the 5'-position. [NIH]

Adenosine Triphosphate: Adenosine 5'-(tetrahydrogen triphosphate). An adenine nucleotide containing three phosphate groups esterified to the sugar moiety. In addition to its crucial roles in metabolism adenosine triphosphate is a neurotransmitter. [NIH]

Adenovirus: A group of viruses that cause respiratory tract and eye infections. Adenoviruses used in gene therapy are altered to carry a specific tumor-fighting gene. [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]

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]

Adoptive Transfer: Form of passive immunization where previously sensitized immunologic agents (cells or serum) are transferred to non-immune recipients. When transfer of cells is used as a therapy for the treatment of neoplasms, it is called adoptive immunotherapy (immunotherapy, adoptive). [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]

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

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]

Agarose: A polysaccharide complex, free of nitrogen and prepared from agar-agar which is produced by certain seaweeds (red algae). It dissolves in warm water to form a viscid solution. [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]

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

Alertness: A state of readiness to detect and respond to certain specified small changes occurring at random intervals in the environment. [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]

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

Allergen: An antigenic substance capable of producing immediate-type hypersensitivity (allergy). [EU]

Allergic Rhinitis: Inflammation of the nasal mucous membrane associated with hay fever; fits may be provoked by substances in the working environment. [NIH]

Allogeneic: Taken from different individuals of the same species. [NIH]

Allograft: An organ or tissue transplant between two humans. [NIH]

Allylamine: Possesses an unusual and selective cytotoxicity for vascular smooth muscle cells in dogs and rats. Useful for experiments dealing with arterial injury, myocardial fibrosis or cardiac decompensation. [NIH]

Alpha Particles: Positively charged particles composed of two protons and two neutrons, i.e., helium nuclei, emitted during disintegration of very heavy isotopes; a beam of alpha particles or an alpha ray has very strong ionizing power, but weak penetrability. [NIH]

Alpha-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]

Altitude Sickness: A morbid condition of anoxia caused by the reduced available oxygen at high altitudes. [NIH]

Aluminum: A metallic element that has the atomic number 13, atomic symbol Al, and atomic weight 26.98. [NIH]

Aluminum Hydroxide: Hydrated aluminum. A compound with many biomedical applications: as a gastric antacid, an antiperspirant, in dentifrices, as an emulsifier, as an adjuvant in bacterins and vaccines, in water purification, etc. [NIH]

Alveolar Process: The thickest and spongiest part of the maxilla and mandible hollowed out into deep cavities for the teeth. [NIH]

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

Amebiasis: Infection with any of various amebae. It is an asymptomatic carrier state in most individuals, but diseases ranging from chronic, mild diarrhea to fulminant dysentery may occur. [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 Acid Substitution: The naturally occurring or experimentally induced replacement of one or more amino acids in a protein with another. If a functionally equivalent amino acid is substituted, the protein may retain wild-type activity. Substitution may also diminish or eliminate protein function. Experimentally induced substitution is often used to study enzyme activities and binding site properties. [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]

Aminocamptothecin: An anticancer drug that belongs to the family of drugs called topoisomerase inhibitors. [NIH]

Amino-terminal: The end of a protein or polypeptide chain that contains a free amino group (-NH2). [NIH]

Ammonia: A colorless alkaline gas. It is formed in the body during decomposition of

organic materials during a large number of metabolically important reactions. [NIH]

Ammonium Sulfate: Sulfuric acid diammonium salt. It is used in fractionation of proteins. [NIH]

Amphetamine: A powerful central nervous system stimulant and sympathomimetic. Amphetamine has multiple mechanisms of action including blocking uptake of adrenergics and dopamine, stimulation of release of monamines, and inhibiting monoamine oxidase. Amphetamine is also a drug of abuse and a psychotomimetic. The l- and the d,l-forms are included here. The l-form has less central nervous system activity but stronger cardiovascular effects. The d-form is dextroamphetamine. [NIH]

Amplification: The production of additional copies of a chromosomal DNA sequence, found as either intrachromosomal or extrachromosomal DNA. [NIH]

Ampulla: A sac-like enlargement of a canal or duct. [NIH]

Amygdala: Almond-shaped group of basal nuclei anterior to the inferior horn of the lateral ventricle of the brain, within the temporal lobe. The amygdala is part of the limbic system. [NIH]

Amylases: A group of amylolytic enzymes that cleave starch, glycogen, and related alpha-1,4-glucans. (Stedman, 25th ed) EC 3.2.1.-. [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]

Anaerobic: 1. Lacking molecular oxygen. 2. Growing, living, or occurring in the absence of molecular oxygen; pertaining to an anaerobe. [EU]

Anaesthesia: Loss of feeling or sensation. Although the term is used for loss of tactile sensibility, or of any of the other senses, it is applied especially to loss of the sensation of pain, as it is induced to permit performance of surgery or other painful procedures. [EU]

Anaesthetic: 1. Pertaining to, characterized by, or producing anaesthesia. 2. A drug or agent that is used to abolish the sensation of pain. [EU]

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

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]

Analogous: Resembling or similar in some respects, as in function or appearance, but not in origin or development;. [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]

Anaplasia: Loss of structural differentiation and useful function of neoplastic cells. [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]

Angiopathy: Disease of the blood vessels (arteries, veins, and capillaries) that occurs when someone has diabetes for a long time. There are two types of angiopathy: macroangiopathy and microangiopathy. In macroangiopathy, fat and blood clots build up in the large blood vessels, stick to the vessel walls, and block the flow of blood. In microangiopathy, the walls of the smaller blood vessels become so thick and weak that they bleed, leak protein, and slow the flow of blood through the body. Then the cells, for example, the ones in the center of the eye, do not get enough blood and may be damaged. [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]

Anionic: Pertaining to or containing an anion. [EU]

Anions: Negatively charged atoms, radicals or groups of atoms which travel to the anode or positive pole during electrolysis. [NIH]

Annealing: The spontaneous alignment of two single DNA strands to form a double helix. [NIH]

Anode: Electrode held at a positive potential with respect to a cathode. [NIH]

Anorectal: Pertaining to the anus and rectum or to the junction region between the two. [EU]

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]

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]

Anthrax: An acute bacterial infection caused by ingestion of bacillus organisms. Carnivores may become infected from ingestion of infected carcasses. It is transmitted to humans by contact with infected animals or contaminated animal products. The most common form in humans is cutaneous anthrax. [NIH]

Anthropometry: The technique that deals with the measurement of the size, weight, and proportions of the human or other primate body. [NIH]

Anti-Anxiety Agents: Agents that alleviate anxiety, tension, and neurotic symptoms, promote sedation, and have a calming effect without affecting clarity of consciousness or neurologic conditions. Some are also effective as anticonvulsants, muscle relaxants, or anesthesia adjuvants. Adrenergic beta-antagonists are commonly used in the symptomatic treatment of anxiety but are not included here. [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]

Antibiotic Prophylaxis: Use of antibiotics before, during, or after a diagnostic, therapeutic, or surgical procedure to prevent infectious complications. [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]

Antidiarrheals: Miscellaneous agents found useful in the symptomatic treatment of diarrhea. They have no effect on the agent(s) that cause diarrhea, but merely alleviate the condition. [NIH]

Antidote: A remedy for counteracting a poison. [EU]

Antiemetic: An agent that prevents or alleviates nausea and vomiting. Also antinauseant. [EU]

Antiepileptic: An agent that combats epilepsy. [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]

Antihypertensive: An agent that reduces high blood pressure. [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]

Antimetabolite: A chemical that is very similar to one required in a normal biochemical reaction in cells. Antimetabolites can stop or slow down the reaction. [NIH]

Antimicrobial: Killing microorganisms, or suppressing their multiplication or growth. [EU]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

Antiprotozoal Agents: Substances that are destructive to protozoans. [NIH]

Antipruritic: Relieving or preventing itching. [EU]

Antispasmodic: An agent that relieves spasm. [EU]

Antitussive: An agent that relieves or prevents cough. [EU]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Anuria: Inability to form or excrete urine. [NIH]

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

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

Apocrine Glands: Large, branched, specialized sweat glands that empty into the upper portion of a hair follicle instead of directly onto the skin. [NIH]

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

Aqueous: Having to do with water. [NIH]

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]

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

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

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]

Articular: Of or pertaining to a joint. [EU]

Ascites: Accumulation or retention of free fluid within the peritoneal cavity. [NIH]

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

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

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]

Astrovirus: A genus of small, circular RNA viruses in the family Astroviridae. They cause gastroenteritis and are found in the stools of several vertebrates including humans. Transmission is by the fecal-oral route. There are at least seven human serotypes and the type species is human astrovirus 1. [NIH]

Asymptomatic: Having no signs or symptoms of disease. [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]

Atrial: Pertaining to an atrium. [EU]

Atrial Fibrillation: Disorder of cardiac rhythm characterized by rapid, irregular atrial impulses and ineffective atrial contractions. [NIH]

Atrioventricular: Pertaining to an atrium of the heart and to a ventricle. [EU]

Atrioventricular Node: A small nodular mass of specialized muscle fibers located in the interatrial septum near the opening of the coronary sinus. It gives rise to the atrioventricular bundle of the conduction system of the heart. [NIH]

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

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]

Atropine: A toxic alkaloid, originally from Atropa belladonna, but found in other plants, mainly Solanaceae. [NIH]

Attenuated: Strain with weakened or reduced virulence. [NIH]

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

Autodigestion: Autolysis; a condition found in disease of the stomach: the stomach wall is digested by the gastric juice. [NIH]

Autologous: Taken from an individual's own tissues, cells, or DNA. [NIH]

Autologous bone marrow transplantation: A procedure in which bone marrow is removed from a person, stored, and then given back to the person after intensive treatment. [NIH]

Autonomic: Self-controlling; functionally independent. [EU]

Autonomic Nervous System: The enteric, parasympathetic, and sympathetic nervous systems taken together. Generally speaking, the autonomic nervous system regulates the internal environment during both peaceful activity and physical or emotional stress. Autonomic activity is controlled and integrated by the central nervous system, especially the hypothalamus and the solitary nucleus, which receive information relayed from visceral afferents; these and related central and sensory structures are sometimes (but not here) considered to be part of the autonomic nervous system itself. [NIH]

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

Avian: A plasmodial infection in birds. [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]

Bacillus: A genus of Bacillaceae that are spore-forming, rod-shaped cells. Most species are saprophytic soil forms with only a few species being pathogenic. [NIH]

Bacteremia: The presence of viable bacteria circulating in the blood. Fever, chills, tachycardia, and tachypnea are common acute manifestations of bacteremia. The majority of cases are seen in already hospitalized patients, most of whom have underlying diseases or procedures which render their bloodstreams susceptible to invasion. [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 Infections: Infections by bacteria, general or unspecified. [NIH]

Bacterial Physiology: Physiological processes and activities of bacteria. [NIH]

Bacterial Proteins: Proteins found in any species of bacterium. [NIH]

Bacterial toxin: A toxic substance, made by bacteria, that can be modified to kill specific tumor cells without harming normal cells. [NIH]

Bactericidal: Substance lethal to bacteria; substance capable of killing bacteria. [NIH]

Bacteriophage: A virus whose host is a bacterial cell; A virus that exclusively infects bacteria. It generally has a protein coat surrounding the genome (DNA or RNA). One of the coliphages most extensively studied is the lambda phage, which is also one of the most important. [NIH]

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

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]

Barium: An element of the alkaline earth group of metals. It has an atomic symbol Ba, atomic number 56, and atomic weight 138. All of its acid-soluble salts are poisonous. [NIH]

Barium enema: A procedure in which a liquid with barium in it is put into the rectum and colon by way of the anus. Barium is a silver-white metallic compound that helps to show the image of the lower gastrointestinal tract on an x-ray. [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]

Base Sequence: The sequence of purines and pyrimidines in nucleic acids and polynucleotides. It is also called nucleotide or nucleoside sequence. [NIH]

Basement Membrane: Ubiquitous supportive tissue adjacent to epithelium and around smooth and striated muscle cells. This tissue contains intrinsic macromolecular components such as collagen, laminin, and sulfated proteoglycans. As seen by light microscopy one of its subdivisions is the basal (basement) lamina. [NIH]

Basophil: A type of white blood cell. Basophils are granulocytes. [NIH]

Belladonna: A species of very poisonous Solanaceous plants yielding atropine (hyoscyamine), scopolamine, and other belladonna alkaloids, used to block the muscarinic autonomic nervous system. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Benzamides: Benzoic acid amides. [NIH]

Berberine: An alkaloid from Hydrastis canadensis L., Berberidaceae. It is also found in many other plants. It is relatively toxic parenterally, but has been used orally for various parasitic and fungal infections and as antidiarrheal. [NIH]

Beta-pleated: Particular three-dimensional pattern of amyloidoses. [NIH]

Beta-Thromboglobulin: A platelet-specific protein which is released when platelets aggregate. Elevated plasma levels have been reported after deep venous thrombosis, pre-eclampsia, myocardial infarction with mural thrombosis, and myeloproliferative disorders. Measurement of beta-thromboglobulin in biological fluids by radioimmunoassay is used for the diagnosis and assessment of progress of thromboembolic disorders. [NIH]

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

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

Bile Acids and Salts: Steroid acids and salts. The primary bile acids are derived from cholesterol in the liver and usually conjugated with glycine or taurine. The secondary bile acids are further modified by bacteria in the intestine. They play an important role in the digestion and absorption of fat. They have also been used pharmacologically, especially in the treatment of gallstones. [NIH]

Bile Ducts: Tubes that carry bile from the liver to the gallbladder for storage and to the small intestine for use in digestion. [NIH]

Bile Pigments: Pigments that give a characteristic color to bile including: bilirubin, biliverdine, and bilicyanin. [NIH]

Biliary: Having to do with the liver, bile ducts, and/or gallbladder. [NIH]

Biliary Tract: The gallbladder and its ducts. [NIH]

Binding agent: A substance that makes a loose mixture stick together. For example, binding agents can be used to make solid pills from loose powders. [NIH]

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

Biogenic Amines: A group of naturally occurring amines derived by enzymatic decarboxylation of the natural amino acids. Many have powerful physiological effects (e.g., histamine, serotonin, epinephrine, tyramine). Those derived from aromatic amino acids, and also their synthetic analogs (e.g., amphetamine), are of use in pharmacology. [NIH]

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]

Biological Warfare: Warfare involving the use of living organisms or their products as disease etiologic agents against people, animals, or plants. [NIH]

Biophysics: The science of physical phenomena and processes in living organisms. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

Biosynthesis: The building up of a chemical compound in the physiologic processes of a living organism. [EU]

Biotechnology: Body of knowledge related to the use of organisms, cells or cell-derived

constituents for the purpose of developing products which are technically, scientifically and clinically useful. Alteration of biologic function at the molecular level (i.e., genetic engineering) is a central focus; laboratory methods used include transfection and cloning technologies, sequence and structure analysis algorithms, computer databases, and gene and protein structure function analysis and prediction. [NIH]

Bioterrorism: The use of biological agents in terrorism. This includes the malevolent use of bacteria, viruses, or toxins against people, animals, or plants. [NIH]

Biotinylation: Incorporation of biotinyl groups into molecules. [NIH]

Bismuth: A metallic element that has the atomic symbol Bi, atomic number 83 and atomic weight 208.98. [NIH]

Bismuth Subsalicylate: A nonprescription medicine such as Pepto-Bismol. Used to treat diarrhea, heartburn, indigestion, and nausea. It is also part of the treatment for ulcers caused by the bacterium Helicobacter pylori (HELL-uh-koh-BAK-tur py-LOH-ree). [NIH]

Bladder: The organ that stores urine. [NIH]

Blast phase: The phase of chronic myelogenous leukemia in which the number of immature, abnormal white blood cells in the bone marrow and blood is extremely high. Also called blast crisis. [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]

Bloating: Fullness or swelling in the abdomen that often occurs after meals. [NIH]

Blood Cell Count: A count of the number of leukocytes and erythrocytes per unit volume in a sample of venous blood. A complete blood count (CBC) also includes measurement of the hemoglobin, hematocrit, and erythrocyte indices. [NIH]

Blood Coagulation: The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [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]

Blood Volume: Volume of circulating blood. It is the sum of the plasma volume and erythrocyte volume. [NIH]

Body Composition: The relative amounts of various components in the body, such as percent body fat. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Body Mass Index: One of the anthropometric measures of body mass; it has the highest correlation with skinfold thickness or body density. [NIH]

Bone Density: The amount of mineral per square centimeter of bone. This is the definition used in clinical practice. Actual bone density would be expressed in grams per milliliter. It is most frequently measured by photon absorptiometry or x-ray computed tomography. [NIH]

Bone Marrow: The soft tissue filling the cavities of bones. Bone marrow exists in two types, yellow and red. Yellow marrow is found in the large cavities of large bones and consists mostly of fat cells and a few primitive blood cells. Red marrow is a hematopoietic tissue and is the site of production of erythrocytes and granular leukocytes. Bone marrow is made up of a framework of connective tissue containing branching fibers with the frame being filled with marrow cells. [NIH]

Bone Marrow Cells: Cells contained in the bone marrow including fat cells, stromal cells, megakaryocytes, and the immediate precursors of most blood cells. [NIH]

Bone Marrow Transplantation: The transference of bone marrow from one human or animal to another. [NIH]

Border Disease: Congenital disorder of lambs caused by a virus closely related to or identical with certain strains of bovine viral diarrhea virus. [NIH]

Border Disease Virus: A species of Pestivirus causing a congenital sheep disease characterized by an abnormally hairy birth-coat, tremors, and poor growth. [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]

Brachytherapy: A collective term for interstitial, intracavity, and surface radiotherapy. It uses small sealed or partly-sealed sources that may be placed on or near the body surface or within a natural body cavity or implanted directly into the tissues. [NIH]

Bradycardia: Excessive slowness in the action of the heart, usually with a heart rate below 60 beats per minute. [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]

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

Breakdown: A physical, metal, or nervous collapse. [NIH]

Breast Feeding: The nursing of an infant at the mother's breast. [NIH]

Breeding: The science or art of changing the constitution of a population of plants or animals through sexual reproduction. [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]

Bronchioles: The tiny branches of air tubes in the lungs. [NIH]

Bronchitis: Inflammation (swelling and reddening) of the bronchi. [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]

Bulking Agents: Laxatives that make bowel movements soft and easy to pass. [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]

Cachexia: General ill health, malnutrition, and weight loss, usually associated with chronic disease. [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]

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 Oxalate: The calcium salt of oxalic acid, occurring in the urine as crystals and in certain calculi. [NIH]

Calicivirus: A genus in the family Caliciviridae containing many species including feline calicivirus , vesicular exanthema of swine virus, and San Miguel sea lion viruses. [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]

Camptothecin: An alkaloid isolated from the stem wood of the Chinese tree, Camptotheca acuminata. This compound selectively inhibits the nuclear enzyme DNA topoisomerase. Several semisynthetic analogs of camptothecin have demonstrated antitumor activity. [NIH]

Campylobacter: A genus of bacteria found in the reproductive organs, intestinal tract, and oral cavity of animals and man. Some species are pathogenic. [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]

Capillary Permeability: Property of blood capillary walls that allows for the selective exchange of substances. Small lipid-soluble molecules such as carbon dioxide and oxygen move freely by diffusion. Water and water-soluble molecules cannot pass through the endothelial walls and are dependent on microscopic pores. These pores show narrow areas (tight junctions) which may limit large molecule movement. [NIH]

Capsaicin: Cytotoxic alkaloid from various species of Capsicum (pepper, paprika), of the Solanaceae. [NIH]

Capsid: The outer protein protective shell of a virus, which protects the viral nucleic acid. [NIH]

Capsules: Hard or soft soluble containers used for the oral administration of medicine. [NIH]

Carbachol: A slowly hydrolyzed cholinergic agonist that acts at both muscarinic and nicotinic receptors. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH2O)n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carbon Dioxide: A colorless, odorless gas that can be formed by the body and is necessary for the respiration cycle of plants and animals. [NIH]

Carcinogen: Any substance that causes cancer. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Carcinoma: Cancer that begins in the skin or in tissues that line or cover internal organs. [NIH]

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

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular Agents: Agents that affect the rate or intensity of cardiac contraction, blood vessel diameter, or blood volume. [NIH]

Cardiovascular System: The heart and the blood vessels by which blood is pumped and circulated through the body. [NIH]

Carnitine: Constituent of striated muscle and liver. It is used therapeutically to stimulate gastric and pancreatic secretions and in the treatment of hyperlipoproteinemias. [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]

Carrier State: The condition of harboring an infective organism without manifesting symptoms of infection. The organism must be readily transmissable to another susceptible host. [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]

Caspase: Enzyme released by the cell at a crucial stage in apoptosis in order to shred all cellular proteins. [NIH]

Castor Oil: Oil obtained from seeds of Ricinus communis that is used as a cathartic and as a plasticizer. [NIH]

Catalyse: To speed up a chemical reaction. [EU]

Cataract: An opacity, partial or complete, of one or both eyes, on or in the lens or capsule, especially an opacity impairing vision or causing blindness. The many kinds of cataract are classified by their morphology (size, shape, location) or etiology (cause and time of occurrence). [EU]

Catecholamine: A group of chemical substances manufactured by the adrenal medulla and secreted during physiological stress. [NIH]

Cations: Postively charged atoms, radicals or groups of atoms which travel to the cathode or negative pole during electrolysis. [NIH]

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

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

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [NIH]

Caveolae: Endocytic/exocytic cell membrane structures rich in glycosphingolipids, cholesterol, and lipid-anchored membrane proteins that function in endocytosis (potocytosis), transcytosis, and signal transduction. Caveolae assume various shapes from open pits to closed vesicles. Caveolar coats are composed of caveolins. [NIH]

Caveolins: The main structural proteins of caveolae. Several distinct genes for caveolins have been identified. [NIH]

Cecum: The beginning of the large intestine. The cecum is connected to the lower part of the small intestine, called the ileum. [NIH]

Ceftriaxone: Broad-spectrum cephalosporin antibiotic with a very long half-life and high penetrability to usually inaccessible infections, including those involving the meninges, eyes, inner ears, and urinary tract. [NIH]

Celecoxib: A drug that reduces pain. Celecoxib belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is being studied for cancer prevention. [NIH]

Celiac Disease: A disease characterized by intestinal malabsorption and precipitated by gluten-containing foods. The intestinal mucosa shows loss of villous structure. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell Count: A count of the number of cells of a specific kind, usually measured per unit volume of sample. [NIH]

Cell Cycle: The complex series of phenomena, occurring between the end of one cell division and the end of the next, by which cellular material is divided between daughter cells. [NIH]

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

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

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

Cell 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 Membrane Structures: Structures which are part of the cell membrane or have cell membrane as a major part of their structure. [NIH]

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

Cell Respiration: The metabolic process of all living cells (animal and plant) in which oxygen is used to provide a source of energy for the cell. [NIH]

Cell Size: The physical dimensions of a cell. It refers mainly to changes in dimensions correlated with physiological or pathological changes in cells. [NIH]

Cell Transplantation: Transference of cells within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Cellular Structures: Components of a cell. [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]

Ceramide: A type of fat produced in the body. It may cause some types of cells to die, and is being studied in cancer treatment. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

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

Cerebral Hemorrhage: Bleeding into a cerebral hemisphere of the brain, including lobar, subcortical white matter, and basal ganglia hemorrhages. Commonly associated conditions include hypertension; intracranial arteriosclerosis; intracranial aneurysm; craniocerebral trauma; intracranial arteriovenous malformations; cerebral amyloid angiopathy; and cerebral infarction. [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]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

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]

Chemokines: Class of pro-inflammatory cytokines that have the ability to attract and activate leukocytes. They can be divided into at least three structural branches: C

(chemokines, C), CC (chemokines, CC), and CXC (chemokines, CXC), according to variations in a shared cysteine motif. [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]

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]

Chlorophyll: Porphyrin derivatives containing magnesium that act to convert light energy in photosynthetic organisms. [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]

Cholestyramine: Strongly basic anion exchange resin whose main constituent is polystyrene trimethylbenzylammonium as Cl(-) anion. It exchanges chloride ions with bile salts, thus decreasing their concentration and that of cholesterol. It is used as a hypocholesteremic in diarrhea and biliary obstruction and as an antipruritic. [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]

Chondroitin sulfate: The major glycosaminoglycan (a type of sugar molecule) in cartilage. [NIH]

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]

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

Chromosomal: Pertaining to chromosomes. [EU]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all

human cells contain 46 chromosomes. [NIH]

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 lymphocytic leukemia: A slowly progressing disease in which too many white blood cells (called lymphocytes) are found in the body. [NIH]

Chronic myelogenous leukemia: CML. A slowly progressing disease in which too many white blood cells are made in the bone marrow. Also called chronic myeloid leukemia or chronic granulocytic leukemia. [NIH]

Chronic Obstructive Pulmonary Disease: Collective term for chronic bronchitis and emphysema. [NIH]

Chronic phase: Refers to the early stages of chronic myelogenous leukemia or chronic lymphocytic leukemia. The number of mature and immature abnormal white blood cells in the bone marrow and blood is higher than normal, but lower than in the accelerated or blast phase. [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]

Cicatricial: Ectropion due to scar tissue on the margins or the surrounding surfaces of the eyelids. [NIH]

Ciliary: Inflammation or infection of the glands of the margins of the eyelids. [NIH]

Ciliary Body: A ring of tissue extending from the scleral spur to the ora serrata of the retina. It consists of the uveal portion and the epithelial portion. The ciliary muscle is in the uveal portion and the ciliary processes are in the epithelial portion. [NIH]

Cimetidine: A histamine congener, it competitively inhibits histamine binding to H2 receptors. Cimetidine has a range of pharmacological actions. It inhibits gastric acid secretion, as well as pepsin and gastrin output. It also blocks the activity of cytochrome P-450. [NIH]

CIS: Cancer Information Service. The CIS is the National Cancer Institute's link to the public, interpreting and explaining research findings in a clear and understandable manner, and providing personalized responses to specific questions about cancer. Access the CIS by calling 1-800-4-CANCER, or by using the Web site at http://cis.nci.nih.gov. [NIH]

Cisplatin: An inorganic and water-soluble platinum complex. After undergoing hydrolysis, it reacts with DNA to produce both intra and interstrand crosslinks. These crosslinks appear to impair replication and transcription of DNA. The cytotoxicity of cisplatin correlates with cellular arrest in the G2 phase of the cell cycle. [NIH]

Clamp: A u-shaped steel rod used with a pin or wire for skeletal traction in the treatment of certain fractures. [NIH]

Claudication: Limping or lameness. [EU]

Clear cell carcinoma: A rare type of tumor of the female genital tract in which the inside of the cells looks clear when viewed under a microscope. [NIH]

Cleave: A double-stranded cut in DNA with a restriction endonuclease. [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]

Clone: The term "clone" has acquired a new meaning. It is applied specifically to the bits of inserted foreign DNA in the hybrid molecules of the population. Each inserted segment originally resided in the DNA of a complex genome amid millions of other DNA segment. [NIH]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Clostridium: A genus of motile or nonmotile gram-positive bacteria of the family Bacillaceae. Many species have been identified with some being pathogenic. They occur in water, soil, and in the intestinal tract of humans and lower animals. [NIH]

Clostridium difficile: A common inhabitant of the colon flora in human infants and sometimes in adults. It produces a toxin that causes pseudomembranous enterocolitis in patients receiving antibiotic therapy. [NIH]

Clot Retraction: Retraction of a clot resulting from contraction of platelet pseudopods attached to fibrin strands that is dependent on the contractile protein thrombosthenin. Used as a measure of platelet function. [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]

Coccidia: A subclass of protozoans commonly parasitic in the epithelial cells of the intestinal tract but also found in the liver and other organs. Its organisms are found in both vertebrates and higher invertebrates and comprise two orders: Eimeriida and Eucoccidiida. [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]

Codons: Any triplet of nucleotides (coding unit) in DNA or RNA (if RNA is the carrier of primary genetic information as in some viruses) that codes for particular amino acid or signals the beginning or end of the message. [NIH]

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

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

Colicins: Bacteriocins elaborated by strains of Escherichia coli and related species. They are proteins or protein-lipopolysaccharide complexes lethal to other strains of the same species. [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]

Collagenous Colitis: A type of colitis. Caused by an abnormal band of collagen, a thread-like protein. [NIH]

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

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

Colonoscopy: Endoscopic examination, therapy or surgery of the luminal surface of the colon. [NIH]

Colorectal: Having to do with the colon or the rectum. [NIH]

Colorectal Cancer: Cancer that occurs in the colon (large intestine) or the rectum (the end of the large intestine). A number of digestive diseases may increase a person's risk of colorectal cancer, including polyposis and Zollinger-Ellison Syndrome. [NIH]

Colostrum: The thin, yellow, serous fluid secreted by the mammary glands during pregnancy and immediately postpartum before lactation begins. It consists of immunologically active substances, white blood cells, water, protein, fat, and carbohydrates. [NIH]

Combination chemotherapy: Treatment using more than one anticancer drug. [NIH]

Combination Therapy: Association of 3 drugs to treat AIDS (AZT + DDC or DDI + protease inhibitor). [NIH]

Combinatorial: A cut-and-paste process that churns out thousands of potentially valuable compounds at once. [NIH]

Communis: Common tendon of the rectus group of muscles that surrounds the optic foramen and a portion of the superior orbital fissure, to the anterior margin of which it is attached at the spina recti lateralis. [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]

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]

Conception: The onset of pregnancy, marked by implantation of the blastocyst; the formation of a viable zygote. [EU]

Conduction: The transfer of sound waves, heat, nervous impulses, or electricity. [EU]

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]

Congestive heart failure: Weakness of the heart muscle that leads to a buildup of fluid in body tissues. [NIH]

Conjugated: Acting or operating as if joined; simultaneous. [EU]

Conjugation: 1. The act of joining together or the state of being conjugated. 2. A sexual process seen in bacteria, ciliate protozoa, and certain fungi in which nuclear material is exchanged during the temporary fusion of two cells (conjugants). In bacterial genetics a form of sexual reproduction in which a donor bacterium (male) contributes some, or all, of its DNA (in the form of a replicated set) to a recipient (female) which then incorporates differing genetic information into its own chromosome by recombination and passes the recombined set on to its progeny by replication. In ciliate protozoa, two conjugants of separate mating types exchange micronuclear material and then separate, each now being a fertilized cell. In certain fungi, the process involves fusion of two gametes, resulting in union of their nuclei and formation of a zygote. 3. In chemistry, the joining together of two compounds to produce another compound, such as the combination of a toxic product with some substance in the body to form a detoxified product, which is then eliminated. [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]

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

Constipation: Infrequent or difficult evacuation of feces. [NIH]

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]

Contamination: The soiling or pollution by inferior material, as by the introduction of organisms into a wound, or sewage into a stream. [EU]

Continuous infusion: The administration of a fluid into a blood vessel, usually over a prolonged period of time. [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]

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]

Conventional therapy: A currently accepted and widely used treatment for a certain type of disease, based on the results of past research. Also called conventional treatment. [NIH]

Conventional treatment: A currently accepted and widely used treatment for a certain type of disease, based on the results of past research. Also called conventional therapy. [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]

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 Circulation: The circulation of blood through the coronary vessels of the heart. [NIH]

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]

Coronavirus: A genus of the family Coronaviridae which causes respiratory or gastrointestinal disease in a variety of vertebrates. [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]

Cost Savings: Reductions in all or any portion of the costs of providing goods or services. Savings may be incurred by the provider or the consumer. [NIH]

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]

Creatinine: A compound that is excreted from the body in urine. Creatinine levels are measured to monitor kidney function. [NIH]

Crowns: A prosthetic restoration that reproduces the entire surface anatomy of the visible natural crown of a tooth. It may be partial (covering three or more surfaces of a tooth) or complete (covering all surfaces). It is made of gold or other metal, porcelain, or resin. [NIH]

Cryptosporidia: A parasite that can cause gastrointestinal infection and diarrhea. [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]

Cyclosporine: A drug used to help reduce the risk of rejection of organ and bone marrow transplants by the body. It is also used in clinical trials to make cancer cells more sensitive to anticancer drugs. [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]

Cytochrome: Any electron transfer hemoprotein having a mode of action in which the transfer of a single electron is effected by a reversible valence change of the central iron atom of the heme prosthetic group between the +2 and +3 oxidation states; classified as cytochromes a in which the heme contains a formyl side chain, cytochromes b, which contain protoheme or a closely similar heme that is not covalently bound to the protein, cytochromes c in which protoheme or other heme is covalently bound to the protein, and cytochromes d in which the iron-tetrapyrrole has fewer conjugated double bonds than the hemes have. Well-known cytochromes have been numbered consecutively within groups and are designated by subscripts (beginning with no subscript), e.g. cytochromes c, c1, C2, . New cytochromes are named according to the wavelength in nanometres of the absorption maximum of the a-band of the iron (II) form in pyridine, e.g., c-555. [EU]

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]

Cytoplasm: The protoplasm of a cell exclusive of that of the nucleus; it consists of a continuous aqueous solution (cytosol) and the organelles and inclusions suspended in it (phaneroplasm), and is the site of most of the chemical activities of the cell. [EU]

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

Cytotoxic: Cell-killing. [NIH]

Cytotoxic chemotherapy: Anticancer drugs that kill cells, especially cancer cells. [NIH]

Cytotoxicity: Quality of being capable of producing a specific toxic action upon cells of special organs. [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]

Day Care: Institutional health care of patients during the day. The patients return home at night. [NIH]

Deamination: The removal of an amino group (NH2) from a chemical compound. [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]

Decongestant: An agent that reduces congestion or swelling. [EU]

Defecation: The normal process of elimination of fecal material from the rectum. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Dehydration: The condition that results from excessive loss of body water. [NIH]

Delavirdine: A potent, non-nucleoside reverse transcriptase inhibitor with activity specific for HIV-1. [NIH]

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

Denaturation: Rupture of the hydrogen bonds by heating a DNA solution and then cooling it rapidly causes the two complementary strands to separate. [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 Abutments: Natural teeth or teeth roots used as anchorage for a fixed or removable denture or other prosthesis (such as an implant) serving the same purpose. [NIH]

Dental 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]

Dentate Gyrus: Gray matter situated above the gyrus hippocampi. It is composed of three layers. The molecular layer is continuous with the hippocampus in the hippocampal fissure. The granular layer consists of closely arranged spherical or oval neurons, called granule cells, whose axons pass through the polymorphic layer ending on the dendrites of pyramidal cells in the hippocampus. [NIH]

Dentifrices: Any preparations used for cleansing teeth; they usually contain an abrasive, detergent, binder and flavoring agent and may exist in the form of liquid, paste or powder; may also contain medicaments and caries preventives. [NIH]

Dentures: An appliance used as an artificial or prosthetic replacement for missing teeth and adjacent tissues. It does not include crowns, dental abutments, nor artificial teeth. [NIH]

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]

Dermatitis: Any inflammation of the skin. [NIH]

DES: Diethylstilbestrol. A synthetic hormone that was prescribed from the early 1940s until 1971 to help women with complications of pregnancy. DES has been linked to an increased risk of clear cell carcinoma of the vagina in daughters of women who used DES. DES may also increase the risk of breast cancer in women who used DES. [NIH]

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]

Developing Countries: Countries in the process of change directed toward economic growth, that is, an increase in production, per capita consumption, and income. The process of economic growth involves better utilization of natural and human resources, which results in a change in the social, political, and economic structures. [NIH]

Dexmedetomidine: A selective inhibitor of receptors, adrenergic alpha-2 that has analgesic and sedative properties. Medetomidine is the other racemic form. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

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

Diaphoresis: Perspiration, especially profuse perspiration. Called also sudoresis. [EU]

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]

Dicyclomine: A muscarinic antagonist used as an antispasmodic and in urinary incontinence. It has little effect on glandular secretion or the cardiovascular system. It does have some local anesthetic properties and is used in gastrointestinal, biliary, and urinary tract spasms. [NIH]

Diencephalon: The paired caudal parts of the prosencephalon from which the thalamus, hypothalamus, epithalamus, and subthalamus are derived. [NIH]

Dietary Fats: Fats present in food, especially in animal products such as meat, meat products, butter, ghee. They are present in lower amounts in nuts, seeds, and avocados. [NIH]

Dietary Fiber: The remnants of plant cell walls that are resistant to digestion by the alimentary enzymes of man. It comprises various polysaccharides and lignins. [NIH]

Dietetics: The study and regulation of the diet. [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 Physiology: Functions and activities of the digestive system as a whole or of any of its parts. [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]

Digestive tract: The organs through which food passes when food is eaten. These organs are

the mouth, esophagus, stomach, small and large intestines, and rectum. [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]

Dimethyl: A volatile metabolite of the amino acid methionine. [NIH]

Diphenoxylate: A meperidine congener used as an antidiarrheal, usually in combination with atropine. At high doses, it acts like morphine. Its unesterified metabolite difenoxin has similar properties and is used similarly. It has little or no analgesic activity. [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 Transmission: The transmission of infectious disease or pathogens. When transmission is within the same species, the mode can be horizontal (disease transmission, horizontal) or vertical (disease transmission, vertical). [NIH]

Disease Transmission, Horizontal: The transmission of infectious disease or pathogens from one individual to another in the same generation. [NIH]

Disease Transmission, Vertical: The transmission of infectious disease or pathogens from one generation to another. It includes transmission in utero or intrapartum by exposure to blood and secretions, and postpartum exposure via breastfeeding. [NIH]

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

Dislocation: The displacement of any part, more especially of a bone. Called also luxation. [EU]

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]

Distention: The state of being distended or enlarged; the act of distending. [EU]

Diuresis: Increased excretion of urine. [EU]

Diverticula: Plural form of diverticulum. [NIH]

Diverticulitis: Inflammation of a diverticulum or diverticula. [NIH]

Diverticulum: A pathological condition manifested as a pouch or sac opening from a tubular or sacular organ. [NIH]

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

Domesticated: Species in which the evolutionary process has been influenced by humans to meet their needs. [NIH]

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]

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

Dose-limiting: Describes side effects of a drug or other treatment that are serious enough to prevent an increase in dose or level of that treatment. [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]

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 Design: The molecular designing of drugs for specific purposes (such as DNA-binding, enzyme inhibition, anti-cancer efficacy, etc.) based on knowledge of molecular properties such as activity of functional groups, molecular geometry, and electronic structure, and also on information cataloged on analogous molecules. Drug design is generally computer-assisted molecular modeling and does not include pharmacokinetics, dosage analysis, or drug administration analysis. [NIH]

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

Drug Tolerance: Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

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

Dumping Syndrome: Gastrointestinal symptoms resulting from an absent or nonfunctioning pylorus. [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]

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]

Dynorphins: A class of opioid peptides including dynorphin A, dynorphin B, and smaller fragments of these peptides. Dynorphins prefer kappa-opioid receptors (receptors, opioid, kappa) and have been shown to play a role as central nervous system transmitters. [NIH]

Dysentery: Any of various disorders marked by inflammation of the intestines, especially of the colon, and attended by pain in the abdomen, tenesmus, and frequent stools containing blood and mucus. Causes include chemical irritants, bacteria, protozoa, or parasitic worms. [EU]

Dyskinesia: Impairment of the power of voluntary movement, resulting in fragmentary or incomplete movements. [EU]

Dyslipidemia: Disorders in the lipoprotein metabolism; classified as hypercholesterolemia, hypertriglyceridemia, combined hyperlipidemia, and low levels of high-density lipoprotein (HDL) cholesterol. All of the dyslipidemias can be primary or secondary. Both elevated levels of low-density lipoprotein (LDL) cholesterol and low levels of HDL cholesterol predispose to premature atherosclerosis. [NIH]

Dysmenorrhea: Painful menstruation. [NIH]

Dysphagia: Difficulty in swallowing. [EU]

Dysphoria: Disquiet; restlessness; malaise. [EU]

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

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

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]

Egg Yolk: Cytoplasm stored in an egg that contains nutritional reserves for the developing embryo. It is rich in polysaccharides, lipids, and proteins. [NIH]

Elasticity: Resistance and recovery from distortion of shape. [NIH]

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

Electrocoagulation: Electrosurgical procedures used to treat hemorrhage (e.g., bleeding ulcers) and to ablate tumors, mucosal lesions, and refractory arrhythmias. [NIH]

Electrolysis: Destruction by passage of a galvanic electric current, as in disintegration of a chemical compound in solution. [NIH]

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

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]

Emaciation: Clinical manifestation of excessive leanness usually caused by disease or a lack of nutrition. [NIH]

Embolus: 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]

Emphysema: A pathological accumulation of air in tissues or organs. [NIH]

Empiric: Empirical; depending upon experience or observation alone, without using scientific method or theory. [EU]

Emulsions: Colloids of two immiscible liquids where either phase may be either fatty or aqueous; lipid-in-water emulsions are usually liquid, like milk or lotion and water-in-lipid emulsions tend to be creams. [NIH]

Encapsulated: Confined to a specific, localized area and surrounded by a thin layer of tissue. [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]

Encephalomyelitis: A general term indicating inflammation of the brain and spinal cord, often used to indicate an infectious process, but also applicable to a variety of autoimmune and toxic-metabolic conditions. There is significant overlap regarding the usage of this term and encephalitis in the literature. [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]

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]

Endocytosis: Cellular uptake of extracellular materials within membrane-limited vacuoles or microvesicles. Endosomes play a central role in endocytosis. [NIH]

Endopeptidases: A subclass of peptide hydrolases. They are classified primarily by their catalytic mechanism. Specificity is used only for identification of individual enzymes. They comprise the serine endopeptidases, EC 3.4.21; cysteine endopeptidases, EC 3.4.22; aspartic endopeptidases, EC 3.4.23, metalloendopeptidases, EC 3.4.24; and a group of enzymes yet to be assigned to any of the above sub-classes, EC 3.4.99. EC 3.4.-. [NIH]

Endorphin: Opioid peptides derived from beta-lipotropin. Endorphin is the most potent naturally occurring analgesic agent. It is present in pituitary, brain, and peripheral tissues. [NIH]

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

Endoscopic: A technique where a lateral-view endoscope is passed orally to the duodenum for visualization of the ampulla of Vater. [NIH]

Endoscopy: Endoscopic examination, therapy or surgery performed on interior parts of the body. [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-derived: Small molecule that diffuses to the adjacent muscle layer and relaxes it. [NIH]

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]

Enema: The injection of a liquid through the anus into the large bowel. [NIH]

Enhancers: Transcriptional element in the virus genome. [NIH]

Enkephalin: A natural opiate painkiller, in the hypothalamus. [NIH]

Enteral Nutrition: Nutritional support given via the alimentary canal or any route connected to the gastrointestinal system (i.e., the enteral route). This includes oral feeding, sip feeding, and tube feeding using nasogastric, gastrostomy, and jejunostomy tubes. [NIH]

Enteric bacteria: Single-celled microorganisms that lack chlorophyll. Some bacteria are capable of causing human, animal, or plant diseases; others are essential in pollution control because they break down organic matter in the air and in the water. [NIH]

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

Enteric-coated: A term designating a special coating applied to tablets or capsules which prevents release and absorption of their contents until they reach the intestines. [EU]

Enteritis: Inflammation of the intestine, applied chiefly to inflammation of the small intestine; see also enterocolitis. [EU]

Enterocolitis: Inflammation of the intestinal mucosa of the small and large bowel. [NIH]

Enterocytes: Terminally differentiated cells comprising the majority of the external surface of the intestinal epithelium (see intestinal mucosa). Unlike goblet cells, they do not produce or secrete mucins, nor do they secrete cryptdins as do the paneth cells. [NIH]

Enterohepatic: Of or involving the intestine and liver. [EU]

Enterohepatic Circulation: Recycling through liver by excretion in bile, reabsorption from intestines into portal circulation, passage back into liver, and re-excretion in bile. [NIH]

Enterostomal Therapy: A nurse who cares for patients with an ostomy. [NIH]

Enterotoxins: Substances that are toxic to the intestinal tract causing vomiting, diarrhea, etc.; most common enterotoxins are produced by bacteria. [NIH]

Entorhinal Cortex: Cortex where the signals are combined with those from other sensory systems. [NIH]

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

Environmental Health: The science of controlling or modifying those conditions, influences, or forces surrounding man which relate to promoting, establishing, and maintaining health. [NIH]

Enzymatic: Phase where enzyme cuts the precursor protein. [NIH]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

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

Eosinophils: Granular leukocytes with a nucleus that usually has two lobes connected by a slender thread of chromatin, and cytoplasm containing coarse, round granules that are uniform in size and stainable by eosin. [NIH]

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

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]

Epigastric: Having to do with the upper middle area of the abdomen. [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]

Epithalamus: The dorsal posterior subdivision of the diencephalon. The epithalamus is generally considered to include the habenular nuclei (habenula) and associated fiber bundles, the pineal body, and the epithelial roof of the third ventricle. The anterior and posterior paraventricular nuclei of the thalamus are included with the thalamic nuclei although they develop from the same pronuclear mass as the epithalamic nuclei and are sometimes considered part of the epithalamus. [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]

Epitope: A molecule or portion of a molecule capable of binding to the combining site of an antibody. For every given antigenic determinant, the body can construct a variety of antibody-combining sites, some of which fit almost perfectly, and others which barely fit. [NIH]

Erythrocyte Indices: Quantification of size and cell hemoglobin content or concentration of the erythrocyte, usually derived from erythrocyte count, blood hemoglobin concentration, and hematocrit. Includes the mean cell volume (MCV), mean cell hemoglobin (MCH), and mean cell hemoglobin concentration (MCHC). Use also for cell diameter and thickness. [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]

Esophageal: Having to do with the esophagus, the muscular tube through which food

passes from the throat to the stomach. [NIH]

Esophagitis: Inflammation, acute or chronic, of the esophagus caused by bacteria, chemicals, or trauma. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [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]

Ether: One of a class of organic compounds in which any two organic radicals are attached directly to a single oxygen atom. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Euphoria: An exaggerated feeling of physical and emotional well-being not consonant with apparent stimuli or events; usually of psychologic origin, but also seen in organic brain disease and toxic states. [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]

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]

Excrete: To get rid of waste from the body. [NIH]

Exhaustion: The feeling of weariness of mind and body. [NIH]

Exocrine: Secreting outwardly, via a duct. [EU]

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]

Expiration: The act of breathing out, or expelling air from the lungs. [EU]

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

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

External-beam radiation: Radiation therapy that uses a machine to aim high-energy rays at the cancer. Also called external radiation. [NIH]

Extracellular: Outside a cell or cells. [EU]

Extracellular Matrix: A meshwork-like substance found within the extracellular space and in association with the basement membrane of the cell surface. It promotes cellular proliferation and provides a supporting structure to which cells or cell lysates in culture dishes adhere. [NIH]

Extracellular Space: Interstitial space between cells, occupied by fluid as well as amorphous and fibrous substances. [NIH]

Extrapyramidal: Outside of the pyramidal tracts. [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]

Eye Infections: Infection, moderate to severe, caused by bacteria, fungi, or viruses, which occurs either on the external surface of the eye or intraocularly with probable inflammation, visual impairment, or blindness. [NIH]

Faecal: Pertaining to or of the nature of feces. [EU]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Family Practice: A medical specialty concerned with the provision of continuing, comprehensive primary health care for the entire family. [NIH]

Famotidine: A competitive histamine H2-receptor antagonist. Its main pharmacodynamic effect is the inhibition of gastric secretion. [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]

Fecal Incontinence: Failure of voluntary control of the anal sphincters, with involuntary passage of feces and flatus. [NIH]

Fecal occult blood test: A test to check for blood in stool. (Fecal refers to stool; occult means hidden.) [NIH]

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]

Fentanyl: A narcotic opioid drug that is used in the treatment of pain. [NIH]

Fermentation: An enzyme-induced chemical change in organic compounds that takes place in the absence of oxygen. The change usually results in the production of ethanol or lactic acid, and the production of energy. [NIH]

Fetal Resorption: Death and resorption of the fetus at any stage after the completion of organogenesis which, in humans, is after the 9th week of gestation. It does not include embryo resorption. [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]

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

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ,

usually as a consequence of inflammation or other injury. [NIH]

Filtration: The passage of a liquid through a filter, accomplished by gravity, pressure, or vacuum (suction). [EU]

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

Flagellin: A protein with a molecular weight of 40,000 isolated from bacterial flagella. At appropriate pH and salt concentration, three flagellin monomers can spontaneously reaggregate to form structures which appear identical to intact flagella. [NIH]

Flagellum: A whiplike appendage of a cell. It can function either as an organ of locomotion or as a device for moving the fluid surrounding the cell. [NIH]

Flatulence: Production or presence of gas in the gastrointestinal tract which may be expelled through the anus. [NIH]

Flatus: Gas passed through the rectum. [NIH]

Flaviviridae: A family of RNA viruses, some formerly classified under Togoviridae, many of which cause disease in humans and domestic animals. The three genera are Flavivirus, Pestivirus, and Hepatitis C-like viruses. [NIH]

Flavivirus: A genus of Flaviviridae, also known as Group B arbovirus, containing several subgroups and species. Most are arboviruses transmitted by mosquitoes or ticks. The type species is yellow fever virus. [NIH]

Flow Cytometry: Technique using an instrument system for making, processing, and displaying one or more measurements on individual cells obtained from a cell suspension. Cells are usually stained with one or more fluorescent dyes specific to cell components of interest, e.g., DNA, and fluorescence of each cell is measured as it rapidly transverses the excitation beam (laser or mercury arc lamp). Fluorescence provides a quantitative measure of various biochemical and biophysical properties of the cell, as well as a basis for cell sorting. Other measurable optical parameters include light absorption and light scattering, the latter being applicable to the measurement of cell size, shape, density, granularity, and stain uptake. [NIH]

Fluid Therapy: Therapy whose basic objective is to restore the volume and composition of the body fluids to normal with respect to water-electrolyte balance. Fluids may be administered intravenously, orally, by intermittent gavage, or by hypodermoclysis. [NIH]

Fluorescence: The property of emitting radiation while being irradiated. The radiation emitted is usually of longer wavelength than that incident or absorbed, e.g., a substance can be irradiated with invisible radiation and emit visible light. X-ray fluorescence is used in diagnosis. [NIH]

Fluorescent Dyes: Dyes that emit light when exposed to light. The wave length of the emitted light is usually longer than that of the incident light. Fluorochromes are substances that cause fluorescence in other substances, i.e., dyes used to mark or label other compounds with fluorescent tags. They are used as markers in biochemistry and immunology. [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]

Fluoroscopy: Production of an image when X-rays strike a fluorescent screen. [NIH]

Fluorouracil: A pyrimidine analog that acts as an antineoplastic antimetabolite and also has immunosuppressant. It interferes with DNA synthesis by blocking the thymidylate synthetase conversion of deoxyuridylic acid to thymidylic acid. [NIH]

Flush: Transient, episodic redness of the face and neck caused by certain diseases, ingestion

of certain drugs or other substances, heat, emotional factors, or physical exertion. [EU]

Flutter: A rapid vibration or pulsation. [EU]

Foam Cells: Lipid-laden macrophages originating from monocytes or from smooth muscle cells. [NIH]

Fold: A plication or doubling of various parts of the body. [NIH]

Folic Acid: N-(4-(((2-Amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl)amino)benzoyl)-L-glutamic acid. A member of the vitamin B family that stimulates the hematopoietic system. It is present in the liver and kidney and is found in mushrooms, spinach, yeast, green leaves, and grasses. Folic acid is used in the treatment and prevention of folate deficiencies and megaloblastic anemia. [NIH]

Food and Beverages: Edible or potable substances. [NIH]

Foodborne Illness: An acute gastrointestinal infection caused by food that contains harmful bacteria. Symptoms include diarrhea, abdominal pain, fever, and chills. Also called food poisoning. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Formularies: Lists of drugs or collections of recipes, formulas, and prescriptions for the compounding of medicinal preparations. Formularies differ from pharmacopoeias in that they are less complete, lacking full descriptions of the drugs, their formulations, analytic composition, chemical properties, etc. In hospitals, formularies list all drugs commonly stocked in the hospital pharmacy. [NIH]

Formulary: A book containing a list of pharmaceutical products with their formulas and means of preparation. [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]

Fractionation: Dividing the total dose of radiation therapy into several smaller, equal doses delivered over a period of several days. [NIH]

Frail Elderly: Older adults or aged individuals who are lacking in general strength and are unusually susceptible to disease or to other infirmity. [NIH]

Frameshift: A type of mutation which causes out-of-phase transcription of the base sequence; such mutations arise from the addition or delection of nucleotide(s) in numbers other than 3 or multiples of 3. [NIH]

Frameshift Mutation: A type of mutation in which a number of nucleotides not divisible by three is deleted from or inserted into a coding sequence, thereby causing an alteration in the reading frame of the entire sequence downstream of the mutation. These mutations may be induced by certain types of mutagens or may occur spontaneously. [NIH]

Frontal Lobe: The anterior part of the cerebral hemisphere. [NIH]

Fucose: Deoxysugar. [NIH]

Fucosyltransferases: Enzymes catalyzing the transfer of fucose from a nucleoside diphosphate fucose to an acceptor molecule which is frequently another carbohydrate, a glycoprotein, or a glycolipid molecule. Elevated activity of some fucosyltransferases in human serum may serve as an indicator of malignancy. The class includes EC 2.4.1.65; EC 2.4.1.68; EC 2.4.1.69; EC 2.4.1.89. [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]

Galanin: A neurotransmitter. [NIH]

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]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Ganglioside: Protein kinase C's inhibitor which reduces ischemia-related brain damage. [NIH]

Gangrenous: A circumscribed, deep-seated, suppurative inflammation of the subcutaneous tissue of the eyelid discharging pus from several points. [NIH]

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]

Gastric Mucosa: Surface epithelium in the stomach that invaginates into the lamina propria, forming gastric pits. Tubular glands, characteristic of each region of the stomach (cardiac, gastric, and pyloric), empty into the gastric pits. The gastric mucosa is made up of several different kinds of cells. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gastritis: Inflammation of the stomach. [EU]

Gastrocolic Reflex: Increase of muscle movement in the gastrointestinal tract when food enters an empty stomach. May cause the urge to have a bowel movement right after eating. [NIH]

Gastroduodenal: Pertaining to or communicating with the stomach and duodenum, as a gastroduodenal fistula. [EU]

Gastroenteritis: An acute inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhoea, abdominal pain, and weakness, which has various causes, including food poisoning due to infection with such organisms as Escherichia coli, Staphylococcus aureus, and Salmonella species; consumption of irritating food or drink; or psychological factors such as anger, stress, and fear. Called also enterogastritis. [EU]

Gastroenterology: A subspecialty of internal medicine concerned with the study of the physiology and diseases of the digestive system and related structures (esophagus, liver, gallbladder, and pancreas). [NIH]

Gastroesophageal Reflux: Reflux of gastric juice and/or duodenal contents (bile acids, pancreatic juice) into the distal esophagus, commonly due to incompetence of the lower esophageal sphincter. Gastric regurgitation is an extension of this process with entry of fluid into the pharynx or mouth. [NIH]

Gastroesophageal Reflux Disease: Flow of the stomach's contents back up into the esophagus. Happens when the muscle between the esophagus and the stomach (the lower esophageal sphincter) is weak or relaxes when it shouldn't. May cause esophagitis. Also called esophageal reflux or reflux esophagitis. [NIH]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [NIH]

Gastrostomy: Creation of an artificial external opening into the stomach for nutritional support or gastrointestinal compression. [NIH]

Gavage: Feeding by a tube passed into the stomach; called also tube feeding. [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]

Gene Library: A large collection of cloned DNA fragments from a given organism, tissue, organ, or cell type. It may contain complete genomic sequences (genomic library) or complementary DNA sequences, the latter being formed from messenger RNA and lacking intron sequences. [NIH]

Genetic Code: The specifications for how information, stored in nucleic acid sequence (base sequence), is translated into protein sequence (amino acid sequence). The start, stop, and order of amino acids of a protein is specified by consecutive triplets of nucleotides called codons (codon). [NIH]

Genetic Engineering: Directed modification of the gene complement of a living organism by such techniques as altering the DNA, substituting genetic material by means of a virus, transplanting whole nuclei, transplanting cell hybrids, etc. [NIH]

Genetic Markers: A phenotypically recognizable genetic trait which can be used to identify a genetic locus, a linkage group, or a recombination event. [NIH]

Genetic testing: Analyzing DNA to look for a genetic alteration that may indicate an increased risk for developing a specific disease or disorder. [NIH]

Genetic transcription: The process by which the genetic information encoded in the gene, represented as a linear sequence of deoxyribonucleotides, is copied into an exactly complementary sequence of ribonucleotides known as messenger RNA. [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]

Genomic Library: A form of gene library containing the complete DNA sequences present in the genome of a given organism. It contrasts with a cDNA library which contains only sequences utilized in protein coding (lacking introns). [NIH]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Germ Cells: The reproductive cells in multicellular organisms. [NIH]

Germ-free: Free of bacteria, disease-causing viruses, and other organisms that can cause infection. [NIH]

Gestation: The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

Giant Cells: Multinucleated masses produced by the fusion of many cells; often associated with viral infections. In AIDS, they are induced when the envelope glycoprotein of the HIV virus binds to the CD4 antigen of uninfected neighboring T4 cells. The resulting syncytium leads to cell death and thus may account for the cytopathic effect of the virus. [NIH]

Giardia: A genus of flagellate intestinal protozoa parasitic in various vertebrates, including humans. Characteristics include the presence of four pairs of flagella arising from a complicated system of axonemes and cysts that are ellipsoidal to ovoidal in shape. [NIH]

Giardia lamblia: A species of parasitic protozoa that attaches itself to the intestinal mucosa and feeds on mucous secretions. The organism is roughly pear-shaped and motility is somewhat erratic, with a slow oscillation about the long axis. Considered for many years to be non-pathogenic and often found in completely asymptomatic individuals, there is presently strong evidence for its pathogenic potential. [NIH]

Giardiasis: An infection of the small intestine caused by the flagellated protozoan Giardia lamblia. It is spread via contaminated food and water and by direct person-to-person contact. [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]

Glomerular: Pertaining to or of the nature of a glomerulus, especially a renal glomerulus. [EU]

Glucans: Polysaccharides composed of repeating glucose units. They can consist of branched or unbranched chains in any linkages. [NIH]

Glucose: D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

Glucose Intolerance: A pathological state in which the fasting plasma glucose level is less than 140 mg per deciliter and the 30-, 60-, or 90-minute plasma glucose concentration following a glucose tolerance test exceeds 200 mg per deciliter. This condition is seen frequently in diabetes mellitus but also occurs with other diseases. [NIH]

Glucuronic Acid: Derivatives of uronic acid found throughout the plant and animal kingdoms. They detoxify drugs and toxins by conjugating with them to form glucuronides in the liver which are more water-soluble metabolites that can be easily eliminated from the body. [NIH]

Glucuronides: Glycosides of glucuronic acid formed by the reaction of uridine diphosphate glucuronic acid with certain endogenous and exogenous substances. Their formation is important for the detoxification of drugs, steroid excretion and bilirubin metabolism to a more water-soluble compound that can be eliminated in the urine and bile. [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]

Glutamine: A non-essential amino acid present abundantly throught the body and is

involved in many metabolic processes. It is synthesized from glutamic acid and ammonia. It is the principal carrier of nitrogen in the body and is an important energy source for many cells. [NIH]

Gluten: The protein of wheat and other grains which gives to the dough its tough elastic character. [EU]

Glycine: A non-essential amino acid. It is found primarily in gelatin and silk fibroin and used therapeutically as a nutrient. It is also a fast inhibitory neurotransmitter. [NIH]

Glycogen: A sugar stored in the liver and muscles. It releases glucose into the blood when cells need it for energy. Glycogen is the chief source of stored fuel in the body. [NIH]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Glycosaminoglycan: A type of long, unbranched polysaccharide molecule. Glycosaminoglycans are major structural components of cartilage and are also found in the cornea of the eye. [NIH]

Glycosidic: Formed by elimination of water between the anomeric hydroxyl of one sugar and a hydroxyl of another sugar molecule. [NIH]

Glycosylation: The chemical or biochemical addition of carbohydrate or glycosyl groups to other chemicals, especially peptides or proteins. Glycosyl transferases are used in this biochemical reaction. [NIH]

Goats: Any of numerous agile, hollow-horned ruminants of the genus Capra, closely related to the sheep. [NIH]

Goblet Cells: Cells of the epithelial lining that produce and secrete mucins. [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]

Gp120: 120-kD HIV envelope glycoprotein which is involved in the binding of the virus to its membrane receptor, the CD4 molecule, found on the surface of certain cells in the body. [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]

Graft Rejection: An immune response with both cellular and humoral components, directed against an allogeneic transplant, whose tissue antigens are not compatible with those of the recipient. [NIH]

Graft-versus-host disease: GVHD. A reaction of donated bone marrow or peripheral stem cells against a person's tissue. [NIH]

Gram-negative: Losing the stain or decolorized by alcohol in Gram's method of staining, a primary characteristic of bacteria having a cell wall composed of a thin layer of peptidoglycan covered by an outer membrane of lipoprotein and lipopolysaccharide. [EU]

Gram-Negative Bacteria: Bacteria which lose crystal violet stain but are stained pink when treated by Gram's method. [NIH]

Gram-positive: Retaining the stain or resisting decolorization by alcohol in Gram's method

of staining, a primary characteristic of bacteria whose cell wall is composed of a thick layer of peptidologlycan with attached teichoic acids. [EU]

Gram-Positive Bacteria: Bacteria which retain the crystal violet stain when treated by Gram's method. [NIH]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Granulomas: Small lumps in tissues caused by inflammation. [NIH]

Groin: The external junctural region between the lower part of the abdomen and the thigh. [NIH]

Growth: The progressive development of a living being or part of an organism from its earliest stage to maturity. [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]

Guinea Pigs: A common name used for the family Caviidae. The most common species is Cavia porcellus which is the domesticated guinea pig used for pets and biomedical research. [NIH]

Gyrus Cinguli: One of the convolutions on the medial surface of the cerebral hemisphere. It surrounds the rostral part of the brain and interhemispheric commissure and forms part of the limbic system. [NIH]

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]

Handwashing: The act of cleansing the hands with water or other liquid, with or without the inclusion of soap or other detergent, for the purpose of removing soil or microorganisms. [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 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 failure: Loss of pumping ability by the heart, often accompanied by fatigue, breathlessness, and excess fluid accumulation in body tissues. [NIH]

Heartburn: Substernal pain or burning sensation, usually associated with regurgitation of gastric juice into the esophagus. [NIH]

Helminths: Commonly known as parasitic worms, this group includes the acanthocephala, nematoda, and platyhelminths. Some authors consider certain species of leeches that can become temporarily parasitic as helminths. [NIH]

Hematocrit: Measurement of the volume of packed red cells in a blood specimen by centrifugation. The procedure is performed using a tube with graduated markings or with automated blood cell counters. It is used as an indicator of erythrocyte status in disease. For example, anemia shows a low hematocrit, polycythemia, high values. [NIH]

Hematopoietic Stem Cell Transplantation: The transference of stem cells from one animal or human to another (allogeneic), or within the same individual (autologous). The source for the stem cells may be the bone marrow or peripheral blood. Stem cell transplantation has been used as an alternative to autologous bone marrow transplantation in the treatment of a variety of neoplasms. [NIH]

Heme: The color-furnishing portion of hemoglobin. It is found free in tissues and as the prosthetic group in many hemeproteins. [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]

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]

Hemoglobinuria: The presence of free hemoglobin in the urine. [NIH]

Hemolytic: A disease that affects the blood and blood vessels. It destroys red blood cells, cells that cause the blood to clot, and the lining of blood vessels. HUS is often caused by the Escherichia coli bacterium in contaminated food. People with HUS may develop acute renal failure. [NIH]

Hemolytic-Uremic Syndrome: Syndrome of hemolytic anemia, thrombocytopenia, and acute renal failure, with pathological finding of thrombotic microangiopathy in kidney and renal cortical necrosis. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Hemorrhoids: Varicosities of the hemorrhoidal venous plexuses. [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]

Hepatic Encephalopathy: A condition that may cause loss of consciousness and coma. It is usually the result of advanced liver disease. Also called hepatic coma. [NIH]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatobiliary: Pertaining to the liver and the bile or the biliary ducts. [EU]

Hepatocellular: Pertaining to or affecting liver cells. [EU]

Hepatocellular carcinoma: A type of adenocarcinoma, the most common type of liver tumor. [NIH]

Hepatocytes: The main structural component of the liver. They are specialized epithelial cells that are organized into interconnected plates called lobules. [NIH]

Hepatology: The field of medicine concerned with the functions and disorders of the liver. [NIH]

Hepatomegaly: Enlargement of 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]

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]

Hidradenitis: The inflammation of a sweat gland (usually of the apocrine type). The condition can be idiopathic or occur as a result of or in association with another underlying condition. Neutrophilic eccrine hidradenitis is a relatively rare variant that has been reported in patients undergoing chemotherapy, usually for non-Hodgkin lymphomas or leukemic conditions. [NIH]

Hidradenitis Suppurativa: A chronic suppurative and cicatricial disease of the apocrine glands occurring chiefly in the axillae in women and in the groin and anal regions in men. It is characterized by poral occlusion with secondary bacterial infection, evolving into abscesses which eventually rupture. As the disease becomes chronic, ulcers appear, sinus tracts enlarge, fistulas develop, and fibrosis and scarring become evident. Hormonal mechanisms are expected in its pathogenesis. [NIH]

Hippocampus: A curved elevation of gray matter extending the entire length of the floor of the temporal horn of the lateral ventricle (Dorland, 28th ed). The hippocampus, subiculum, and dentate gyrus constitute the hippocampal formation. Sometimes authors include the entorhinal cortex in the hippocampal formation. [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]

Histamine Release: The secretion of histamine from mast cell and basophil granules by exocytosis. This can be initiated by a number of factors, all of which involve binding of IgE, cross-linked by antigen, to the mast cell or basophil's Fc receptors. Once released, histamine binds to a number of different target cell receptors and exerts a wide variety of effects. [NIH]

Histidine: An essential amino acid important in a number of metabolic processes. It is required for the production of histamine. [NIH]

Hog Cholera: An acute, highly contagious disease affecting swine of all ages and caused by the hog cholera virus. It has a sudden onset with high morbidity and mortality. [NIH]

Hog Cholera Virus: A species of the Pestivirus genus causing exceedingly contagious and fatal hemorrhagic disease of swine. [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]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormonal therapy: Treatment of cancer by removing, blocking, or adding hormones. Also called hormone therapy or endocrine therapy. [NIH]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Host: Any animal that receives a transplanted graft. [NIH]

Humoral: Of, relating to, proceeding from, or involving a bodily humour - now often used of endocrine factors as opposed to neural or somatic. [EU]

Humour: 1. A normal functioning fluid or semifluid of the body (as the blood, lymph or bile) especially of vertebrates. 2. A secretion that is itself an excitant of activity (as certain hormones). [EU]

Hybrid: Cross fertilization between two varieties or, more usually, two species of vines, see also crossing. [NIH]

Hydration: Combining with water. [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]

Hydrogen Peroxide: A strong oxidizing agent used in aqueous solution as a ripening agent, bleach, and topical anti-infective. It is relatively unstable and solutions deteriorate over time unless stabilized by the addition of acetanilide or similar organic materials. [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]

Hydroxylysine: A hydroxylated derivative of the amino acid lysine that is present in certain collagens. [NIH]

Hydroxyproline: A hydroxylated form of the imino acid proline. A deficiency in ascorbic acid can result in impaired hydroxyproline formation. [NIH]

Hygienic: Pertaining to hygiene, or conducive to health. [EU]

Hyperalgesia: Excessive sensitiveness or sensibility to pain. [EU]

Hyperbilirubinemia: Pathologic process consisting of an abnormal increase in the amount of bilirubin in the circulating blood, which may result in jaundice. [NIH]

Hypercholesterolemia: Abnormally high levels of cholesterol in the blood. [NIH]

Hyperlipidemia: An excess of lipids in the blood. [NIH]

Hyperphagia: Ingestion of a greater than optimal quantity of food. [NIH]

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]

Hyperthyroidism: Excessive functional activity of the thyroid gland. [NIH]

Hypertriglyceridemia: Condition of elevated triglyceride concentration in the blood; an inherited form occurs in familial hyperlipoproteinemia IIb and hyperlipoproteinemia type IV. It has been linked to higher risk of heart disease and arteriosclerosis. [NIH]

Hypertrophy: General increase in bulk of a part or organ, not due to tumor formation, nor to an increase in the number of cells. [NIH]

Hypnotic: A drug that acts to induce sleep. [EU]

Hypodermic: Applied or administered beneath the skin. [EU]

Hypoglycemic: An orally active drug that produces a fall in blood glucose concentration. [NIH]

Hypoglycemic Agents: Agents which lower the blood glucose level. [NIH]

Hypotension: Abnormally low blood pressure. [NIH]

Hypotensive: Characterized by or causing diminished tension or pressure, as abnormally low blood pressure. [EU]

Hypothalamus: Ventral part of the diencephalon extending from the region of the optic chiasm to the caudal border of the mammillary bodies and forming the inferior and lateral walls of the third ventricle. [NIH]

Hypothyroidism: Deficiency of thyroid activity. In adults, it is most common in women and is characterized by decrease in basal metabolic rate, tiredness and lethargy, sensitivity to cold, and menstrual disturbances. If untreated, it progresses to full-blown myxoedema. In infants, severe hypothyroidism leads to cretinism. In juveniles, the manifestations are intermediate, with less severe mental and developmental retardation and only mild symptoms of the adult form. When due to pituitary deficiency of thyrotropin secretion it is called secondary hypothyroidism. [EU]

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]

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]

Ileal: Related to the ileum, the lowest end of the small intestine. [NIH]

Ileitis: Inflammation of the ileum. [EU]

Ileostomy: Surgical creation of an external opening into the ileum for fecal diversion or drainage. Loop or tube procedures are most often employed. [NIH]

Ileum: The lower end of the small intestine. [NIH]

Ileus: Obstruction of the intestines. [EU]

Imidazole: C3H4N2. The ring is present in polybenzimidazoles. [NIH]

Immune function: Production and action of cells that fight disease or infection. [NIH]

Immune response: The activity of the immune system against foreign substances (antigens). [NIH]

Immune Sera: Serum that contains antibodies. It is obtained from an animal that has been immunized either by antigen injection or infection with microorganisms containing the antigen. [NIH]

Immune system: The organs, cells, and molecules responsible for the recognition and disposal of foreign ("non-self") material which enters the body. [NIH]

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]

Immunoassay: Immunochemical assay or detection of a substance by serologic or immunologic methods. Usually the substance being studied serves as antigen both in antibody production and in measurement of antibody by the test substance. [NIH]

Immunocompetence: The ability of lymphoid cells to mount a humoral or cellular immune response when challenged by antigen. [NIH]

Immunocompromised: Having a weakened immune system caused by certain diseases or treatments. [NIH]

Immunocompromised Host: A human or animal whose immunologic mechanism is deficient because of an immunodeficiency disorder or other disease or as the result of the administration of immunosuppressive drugs or radiation. [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]

Immunodiffusion: Technique involving the diffusion of antigen or antibody through a semisolid medium, usually agar or agarose gel, with the result being a precipitin reaction. [NIH]

Immunoelectrophoresis: A technique that combines protein electrophoresis and double immunodiffusion. In this procedure proteins are first separated by gel electrophoresis (usually agarose), then made visible by immunodiffusion of specific antibodies. A distinct elliptical precipitin arc results for each protein detectable by the antisera. [NIH]

Immunogen: A substance that is capable of causing antibody formation. [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]

Immunosuppressant: An agent capable of suppressing immune responses. [EU]

Immunosuppressive: Describes the ability to lower immune system responses. [NIH]

Immunosuppressive therapy: Therapy used to decrease the body's immune response, such as drugs given to prevent transplant rejection. [NIH]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

Implant radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called [NIH]

In situ: In the natural or normal place; confined to the site of origin without invasion of neighbouring tissues. [EU]

In 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]

Incompetence: Physical or mental inadequacy or insufficiency. [EU]

Incontinence: Inability to control the flow of urine from the bladder (urinary incontinence) or the escape of stool from the rectum (fecal incontinence). [NIH]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

Indigestion: Poor digestion. Symptoms include heartburn, nausea, bloating, and gas. Also called dyspepsia. [NIH]

Indinavir: A potent and specific HIV protease inhibitor that appears to have good oral bioavailability. [NIH]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Infancy: The period of complete dependency prior to the acquisition of competence in walking, talking, and self-feeding. [NIH]

Infantile: Pertaining to an infant or to infancy. [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]

Infectious Diarrhea: Diarrhea caused by infection from bacteria, viruses, or parasites. [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]

Infestation: Parasitic attack or subsistence on the skin and/or its appendages, as by insects, mites, or ticks; sometimes used to denote parasitic invasion of the organs and tissues, as by helminths. [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]

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]

Inlay: In dentistry, a filling first made to correspond with the form of a dental cavity and then cemented into the cavity. [NIH]

Inner ear: The labyrinth, comprising the vestibule, cochlea, and semicircular canals. [NIH]

Inorganic: Pertaining to substances not of organic origin. [EU]

Inositol: An isomer of glucose that has traditionally been considered to be a B vitamin although it has an uncertain status as a vitamin and a deficiency syndrome has not been identified in man. (From Martindale, The Extra Pharmacopoeia, 30th ed, p1379) Inositol phospholipids are important in signal transduction. [NIH]

Inositol 1,4,5-Trisphosphate: Intracellular messenger formed by the action of phospholipase C on phosphatidylinositol 4,5-bisphosphate, which is one of the phospholipids that make up the cell membrane. Inositol 1,4,5-trisphosphate is released into the cytoplasm where it releases calcium ions from internal stores within the cell's endoplasmic reticulum. These calcium ions stimulate the activity of B kinase or calmodulin. [NIH]

Inotropic: Affecting the force or energy of muscular contractions. [EU]

Inpatients: Persons admitted to health facilities which provide board and room, for the purpose of observation, care, diagnosis or treatment. [NIH]

Insight: The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Insomnia: Difficulty in going to sleep or getting enough sleep. [NIH]

Institutionalization: The caring for individuals in institutions and their adaptation to routines characteristic of the institutional environment, and/or their loss of adaptation to life outside the institution. [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]

Interferon: A biological response modifier (a substance that can improve the body's natural response to disease). Interferons interfere with the division of cancer cells and can slow tumor growth. There are several types of interferons, including interferon-alpha, -beta, and -gamma. These substances are normally produced by the body. They are also made in the laboratory for use in treating cancer and other diseases. [NIH]

Interferon-alpha: One of the type I interferons produced by peripheral blood leukocytes or lymphoblastoid cells when exposed to live or inactivated virus, double-stranded RNA, or bacterial products. It is the major interferon produced by virus-induced leukocyte cultures and, in addition to its pronounced antiviral activity, it causes activation of NK cells. [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]

Interleukin-8: A cytokine that activates neutrophils and attracts neutrophils and T-lymphocytes. It is released by several cell types including monocytes, macrophages, T-lymphocytes, fibroblasts, endothelial cells, and keratinocytes by an inflammatory stimulus. IL-8 is a member of the beta-thromboglobulin superfamily and structurally related to platelet factor 4. [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]

Internal radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called brachytherapy, implant radiation, or interstitial radiation therapy. [NIH]

Interphase: The interval between two successive cell divisions during which the chromosomes are not individually distinguishable and DNA replication occurs. [NIH]

Interstitial: Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

Intervention Studies: Epidemiologic investigations designed to test a hypothesized cause-effect relation by modifying the supposed causal factor(s) in the study population. [NIH]

Intervertebral: Situated between two contiguous vertebrae. [EU]

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]

Intracellular Membranes: Membranes of subcellular structures. [NIH]

Intracranial Aneurysm: A saclike dilatation of the walls of a blood vessel, usually an artery. [NIH]

Intracranial Arteriosclerosis: Vascular diseases characterized by thickening, hardening, and remodeling of the walls of intracranial arteries. There are three subtypes: (1) atherosclerosis, marked by fatty depositions in the innermost layer of the arterial walls, (2) Monckeberg's sclerosis, which features calcium deposition in the media and (3) arteriolosclerosis, which refers to sclerosis of small caliber arteries. Clinically, this process may be associated with transient ischemic attack, brain infarction, intracranial embolism and thrombosis, or intracranial aneurysm. [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]

Intramuscular: IM. Within or into muscle. [NIH]

Intraocular: Within the eye. [EU]

Intraocular pressure: Pressure of the fluid inside the eye; normal IOP varies among individuals. [NIH]

Intravenous: IV. Into a vein. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

Introns: Non-coding, intervening sequences of DNA that are transcribed, but are removed from within the primary gene transcript and rapidly degraded during maturation of messenger RNA. Most genes in the nuclei of eukaryotes contain introns, as do mitochondrial and chloroplast genes. [NIH]

Intussusception: A rare disorder. A part of the intestines folds into another part of the intestines, causing blockage. Most common in infants. Can be treated with an operation. [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]

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]

Ion Transport: The movement of ions across energy-transducing cell membranes. Transport can be active or passive. Passive ion transport (facilitated diffusion) derives its energy from the concentration gradient of the ion itself and allows the transport of a single solute in one direction (uniport). Active ion transport is usually coupled to an energy-yielding chemical or photochemical reaction such as ATP hydrolysis. This form of primary active transport is called an ion pump. Secondary active transport utilizes the voltage and ion gradients produced by the primary transport to drive the cotransport of other ions or molecules. These may be transported in the same (symport) or opposite (antiport) direction. [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]

Irinotecan: An anticancer drug that belongs to a family of anticancer drugs called topoisomerase inhibitors. It is a camptothecin analogue. Also called CPT 11. [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]

Jaundice: A clinical manifestation of hyperbilirubinemia, consisting of deposition of bile pigments in the skin, resulting in a yellowish staining of the skin and mucous membranes. [NIH]

Jejunostomy: Surgical formation of an opening through the abdominal wall into the jejunum, usually for enteral hyperalimentation. [NIH]

Joint: The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

Kallidin: A decapeptide bradykinin homolog produced by the action of tissue and glandular kallikreins on low-molecular-weight kininogen. It is a smooth-muscle stimulant and hypotensive agent that functions through vasodilatation. [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]

Keratinocytes: Epidermal cells which synthesize keratin and undergo characteristic changes as they move upward from the basal layers of the epidermis to the cornified (horny) layer of the skin. Successive stages of differentiation of the keratinocytes forming the epidermal layers are basal cell, spinous or prickle cell, and the granular cell. [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 Failure: The inability of a kidney to excrete metabolites at normal plasma levels under conditions of normal loading, or the inability to retain electrolytes under conditions of normal intake. In the acute form (kidney failure, acute), it is marked by uremia and usually by oliguria or anuria, with hyperkalemia and pulmonary edema. The chronic form (kidney failure, chronic) is irreversible and requires hemodialysis. [NIH]

Kidney Failure, Acute: A clinical syndrome characterized by a sudden decrease in glomerular filtration rate, often to values of less than 1 to 2 ml per minute. It is usually associated with oliguria (urine volumes of less than 400 ml per day) and is always associated with biochemical consequences of the reduction in glomerular filtration rate such as a rise in blood urea nitrogen (BUN) and serum creatinine concentrations. [NIH]

Kidney Failure, Chronic: An irreversible and usually progressive reduction in renal function in which both kidneys have been damaged by a variety of diseases to the extent that they are unable to adequately remove the metabolic products from the blood and regulate the body's electrolyte composition and acid-base balance. Chronic kidney failure requires hemodialysis or surgery, usually kidney transplantation. [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]

Kidney Transplantation: The transference of a kidney from one human or animal to another. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Labile: 1. Gliding; moving from point to point over the surface; unstable; fluctuating. 2. Chemically unstable. [EU]

Laceration: 1. The act of tearing. 2. A torn, ragged, mangled wound. [EU]

Lactation: The period of the secretion of milk. [EU]

Lactobacillus: A genus of gram-positive, microaerophilic, rod-shaped bacteria occurring widely in nature. Its species are also part of the many normal flora of the mouth, intestinal tract, and vagina of many mammals, including humans. Pathogenicity from this genus is rare. [NIH]

Lactose Intolerance: The disease state resulting from the absence of lactase enzyme in the musocal cells of the gastrointestinal tract, and therefore an inability to break down the disaccharide lactose in milk for absorption from the gastrointestinal tract. It is manifested by indigestion of a mild nature to severe diarrhea. It may be due to inborn defect genetically conditioned or may be acquired. [NIH]

Lactulose: A mild laxative. [NIH]

Large Intestine: The part of the intestine that goes from the cecum to the rectum. The large intestine absorbs water from stool and changes it from a liquid to a solid form. The large intestine is 5 feet long and includes the appendix, cecum, colon, and rectum. Also called colon. [NIH]

Laxative: An agent that acts to promote evacuation of the bowel; a cathartic or purgative. [EU]

Lectin: A complex molecule that has both protein and sugars. Lectins are able to bind to the outside of a cell and cause biochemical changes in it. Lectins are made by both animals and plants. [NIH]

Length of Stay: The period of confinement of a patient to a hospital or other health facility. [NIH]

Lens: The transparent, double convex (outward curve on both sides) structure suspended between the aqueous and vitreous; helps to focus light on the retina. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Lethal: Deadly, fatal. [EU]

Lethargy: Abnormal drowsiness or stupor; a condition of indifference. [EU]

Leucovorin: The active metabolite of folic acid. Leucovorin is used principally as its calcium salt as an antidote to folic acid antagonists which block the conversion of folic acid to folinic acid. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Leukocytes: White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

Leukocytosis: A transient increase in the number of leukocytes in a body fluid. [NIH]

Leukotrienes: A family of biologically active compounds derived from arachidonic acid by oxidative metabolism through the 5-lipoxygenase pathway. They participate in host defense reactions and pathophysiological conditions such as immediate hypersensitivity and inflammation. They have potent actions on many essential organs and systems, including the cardiovascular, pulmonary, and central nervous system as well as the gastrointestinal tract and the immune system. [NIH]

Library Services: Services offered to the library user. They include reference and circulation. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and

strengthen joints. [EU]

Ligands: A RNA simulation method developed by the MIT. [NIH]

Limbic: Pertaining to a limbus, or margin; forming a border around. [EU]

Limbic System: A set of forebrain structures common to all mammals that is defined functionally and anatomically. It is implicated in the higher integration of visceral, olfactory, and somatic information as well as homeostatic responses including fundamental survival behaviors (feeding, mating, emotion). For most authors, it includes the amygdala, epithalamus, gyrus cinguli, hippocampal formation (see hippocampus), hypothalamus, parahippocampal gyrus, septal nuclei, anterior nuclear group of thalamus, and portions of the basal ganglia. (Parent, Carpenter's Human Neuroanatomy, 9th ed, p744; NeuroNames, http://rprcsgi.rprc.washington.edu/neuronames/index.html (September 2, 1998)). [NIH]

Lincomycin: (2S-trans)-Methyl 6,8-dideoxy-6-(((1-methyl-4-propyl-2-pyrrolidinyl)carbonyl)amino)-1-thio-D-erythro-alpha-D-galacto-octopyranoside. An antibiotic produced by Streptomyces lincolnensis var. lincolnensis. It has been used in the 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]

Lipase: An enzyme of the hydrolase class that catalyzes the reaction of triacylglycerol and water to yield diacylglycerol and a fatty acid anion. It is produced by glands on the tongue and by the pancreas and initiates the digestion of dietary fats. (From Dorland, 27th ed) EC 3.1.1.3. [NIH]

Lipid: Fat. [NIH]

Lipophilic: Having an affinity for fat; pertaining to or characterized by lipophilia. [EU]

Lipopolysaccharide: Substance consisting of polysaccaride and lipid. [NIH]

Lipoprotein: Any of the lipid-protein complexes in which lipids are transported in the blood; lipoprotein particles consist of a spherical hydrophobic core of triglycerides or cholesterol esters surrounded by an amphipathic monolayer of phospholipids, cholesterol, and apolipoproteins; the four principal classes are high-density, low-density, and very-low-density lipoproteins and chylomicrons. [EU]

Liposome: A spherical particle in an aqueous medium, formed by a lipid bilayer enclosing an aqueous compartment. [EU]

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]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

Lobe: A portion of an organ such as the liver, lung, breast, or brain. [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]

Locus Coeruleus: Bluish region in the superior angle of the fourth ventricle floor, corresponding to melanin-like pigmented nerve cells which lie lateral to the ponto-mesencephalic central gray (griseum centrale). It is also known as nucleus pigmentosus pontis. [NIH]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

Loperamide: 4-(p-Chlorophenyl)-4-hydroxy-N.N-dimethyl-alpha,alpha-diphenyl-1-piperidine butyramide hydrochloride. Synthetic anti-diarrheal agent with a long duration of action; it is not significantly absorbed from the gut, has no effect on the adrenergic system or central nervous system, but may antagonize histamine and interfere with acetylcholine release locally. [NIH]

Loperamide hydrochloride: An antidiarrheal drug. [NIH]

Low-density lipoprotein: Lipoprotein that contains most of the cholesterol in the blood. LDL carries cholesterol to the tissues of the body, including the arteries. A high level of LDL increases the risk of heart disease. LDL typically contains 60 to 70 percent of the total serum cholesterol and both are directly correlated with CHD risk. [NIH]

Lower Esophageal Sphincter: The muscle between the esophagus and stomach. When a person swallows, this muscle relaxes to let food pass from the esophagus to the stomach. It stays closed at other times to keep stomach contents from flowing back into the esophagus. [NIH]

Lubricants: Oily or slippery substances. [NIH]

Lumen: The cavity or channel within a tube or tubular organ. [EU]

Luxation: The displacement of the particular surface of a bone from its normal joint, without fracture. [NIH]

Lymph: The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

Lymph node: A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Also known as a lymph gland. Lymph nodes are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic fluid (lymph). [NIH]

Lymphatic: The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases. [NIH]

Lymphocyte Count: A count of the number of lymphocytes in the blood. [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]

Lymphoproliferative: Disorders characterized by proliferation of lymphoid tissue, general or unspecified. [NIH]

Lytic: 1. Pertaining to lysis or to a lysin. 2. Producing lysis. [EU]

Macronutrients: Nutrients in the diet that are the key sources of energy, namely protein, fat, and carbohydrates. [NIH]

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]

Malabsorption: Impaired intestinal absorption of nutrients. [EU]

Malabsorption syndrome: A group of symptoms such as gas, bloating, abdominal pain, and diarrhea resulting from the body's inability to properly absorb nutrients. [NIH]

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]

Malignancy: A cancerous tumor that can invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malnutrition: A condition caused by not eating enough food or not eating a balanced diet. [NIH]

Mammary: Pertaining to the mamma, or breast. [EU]

Mandible: The largest and strongest bone of the face constituting the lower jaw. It supports the lower teeth. [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]

Mastitis: Inflammatory disease of the breast, or mammary gland. [NIH]

Maximum Tolerated Dose: The highest dose level eliciting signs of toxicity without having major effects on survival relative to the test in which it is used. [NIH]

Measles Virus: The type species of morbillivirus and the cause of the highly infectious human disease measles, which affects mostly children. [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]

Mechanical ventilation: Use of a machine called a ventilator or respirator to improve the exchange of air between the lungs and the atmosphere. [NIH]

Medetomidine: An agonist of receptors, adrenergic alpha-2 that is used in veterinary medicine for its analgesic and sedative properties. It is the racemate of dexmedetomidine. [NIH]

Medial: Lying near the midsaggital plane of the body; opposed to lateral. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

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 oncologist: A doctor who specializes in diagnosing and treating cancer using chemotherapy, hormonal therapy, and biological therapy. A medical oncologist often serves as the main caretaker of someone who has cancer and coordinates treatment provided by other specialists. [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]

Megakaryocytes: Very large bone marrow cells which release mature blood platelets. [NIH]

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]

Melanin: The substance that gives the skin its color. [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 Microdomains: Detergent-insoluble cell membrane components. They are

enriched in sphingolipids and cholesterol and clustered with glycosyl-phosphatidylinositol (GPI)-anchored proteins. [NIH]

Membrane Proteins: Proteins which are found in membranes including cellular and intracellular membranes. They consist of two types, peripheral and integral proteins. They include most membrane-associated enzymes, antigenic proteins, transport proteins, and drug, hormone, and lectin receptors. [NIH]

Memory: Complex mental function having four distinct phases: (1) memorizing or learning, (2) retention, (3) recall, and (4) recognition. Clinically, it is usually subdivided into immediate, recent, and remote memory. [NIH]

Meninges: The three membranes that cover and protect the brain and spinal cord. [NIH]

Menopause: Permanent cessation of 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]

Mentors: Senior professionals who provide guidance, direction and support to those persons desirous of improvement in academic positions, administrative positions or other career development situations. [NIH]

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]

Mercury: A silver metallic element that exists as a liquid at room temperature. It has the atomic symbol Hg (from hydrargyrum, liquid silver), atomic number 80, and atomic weight 200.59. Mercury is used in many industrial applications and its salts have been employed therapeutically as purgatives, antisyphilitics, disinfectants, and astringents. It can be absorbed through the skin and mucous membranes which leads to mercury poisoning. Because of its toxicity, the clinical use of mercury and mercurials is diminishing. [NIH]

Mesencephalic: Ipsilateral oculomotor paralysis and contralateral tremor, spasm. or choreic movements of the face and limbs. [NIH]

Mesenteric: Pertaining to the mesentery : a membranous fold attaching various organs to the body wall. [EU]

Mesenteric Lymphadenitis: Inflammation of the mesenteric lymph nodes. [NIH]

Mesentery: A layer of the peritoneum which attaches the abdominal viscera to the abdominal wall and conveys their blood vessels and nerves. [NIH]

Mesocolon: The fold of peritoneum by which the colon is attached to the posterior abdominal wall. [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]

Metaphase: The second phase of cell division, in which the chromosomes line up across the

equatorial plane of the spindle prior to separation. [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]

Metoclopramide: A dopamine D2 antagonist that is used as an antiemetic. [NIH]

Metronidazole: Antiprotozoal used in amebiasis, trichomoniasis, giardiasis, and as treponemacide in livestock. It has also been proposed as a radiation sensitizer for hypoxic cells. According to the Fourth Annual Report on Carcinogens (NTP 85-002, 1985, p133), this substance may reasonably be anticipated to be a carcinogen (Merck, 11th ed). [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]

Micronutrients: Essential dietary elements or organic compounds that are required in only small quantities for normal physiologic processes to occur. [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]

Microsporidiosis: Infections with protozoa of the phylum Microspora. [NIH]

Microtubule-Associated Proteins: High molecular weight proteins found in the microtubules of the cytoskeletal system. Under certain conditions they are required for tubulin assembly into the microtubules and stabilize the assembled microtubules. [NIH]

Microtubules: Slender, cylindrical filaments found in the cytoskeleton of plant and animal cells. They are composed of the protein tubulin. [NIH]

Microvilli: Minute projections of cell membranes which greatly increase the surface area of the cell. [NIH]

Microvillus: A minute process or protrusion from the free surface of a cell. [EU]

Micturition: The passage of urine; urination. [EU]

Migration: The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

Milligram: A measure of weight. A milligram is approximately 450,000-times smaller than a pound and 28,000-times smaller than an ounce. [NIH]

Milliliter: A measure of volume for a liquid. A milliliter is approximately 950-times smaller than a quart and 30-times smaller than a fluid ounce. A milliliter of liquid and a cubic

centimeter (cc) of liquid are the same. [NIH]

Mitochondrial Swelling: Increase in volume of mitochondria due to an influx of fluid; it occurs in hypotonic solutions due to osmotic pressure and in isotonic solutions as a result of altered permeability of the membranes of respiring mitochondria. [NIH]

Mitogen-Activated Protein Kinase Kinases: A serine-threonine protein kinase family whose members are components in protein kinase cascades activated by diverse stimuli. These MAPK kinases phosphorylate mitogen-activated protein kinases and are themselves phosphorylated by MAP kinase kinase kinases. JNK kinases (also known as SAPK kinases) are a subfamily. EC 2.7.10.- [NIH]

Mitogen-Activated Protein Kinases: A superfamily of protein-serine-threonine kinases that are activated by diverse stimuli via protein kinase cascades. They are the final components of the cascades, activated by phosphorylation by mitogen-activated protein kinase kinases which in turn are activated by mitogen-activated protein kinase kinase kinases (MAP kinase kinase kinases). Families of these mitogen-activated protein kinases (MAPKs) include extracellular signal-regulated kinases (ERKs), stress-activated protein kinases (SAPKs) (also known as c-jun terminal kinases (JNKs)), and p38-mitogen-activated protein kinases. EC 2,7,1.- [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]

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]

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]

Monoamine: Enzyme that breaks down dopamine in the astrocytes and microglia. [NIH]

Monoamine Oxidase: An enzyme that catalyzes the oxidative deamination of naturally occurring monoamines. It is a flavin-containing enzyme that is localized in mitochondrial membranes, whether in nerve terminals, the liver, or other organs. Monoamine oxidase is important in regulating the metabolic degradation of catecholamines and serotonin in neural or target tissues. Hepatic monoamine oxidase has a crucial defensive role in inactivating circulating monoamines or those, such as tyramine, that originate in the gut and are absorbed into the portal circulation. (From Goodman and Gilman's, The Pharmacological Basis of Therapeutics, 8th ed, p415) EC 1.4.3.4. [NIH]

Monoclonal: An antibody produced by culturing a single type of cell. It therefore consists of a single species of immunoglobulin molecules. [NIH]

Monoclonal antibodies: Laboratory-produced substances that can locate and bind to cancer cells wherever they are in the body. Many monoclonal antibodies are used in cancer detection or therapy; each one recognizes a different protein on certain cancer cells. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to a tumor. [NIH]

Monocytes: Large, phagocytic mononuclear leukocytes produced in the vertebrate bone marrow and released into the blood; contain a large, oval or somewhat indented nucleus surrounded by voluminous cytoplasm and numerous organelles. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Morbillivirus: A genus of the family Paramyxoviridae (subfamily Paramyxovirinae) where all the virions have hemagglutinin but not neuraminidase activity. All members produce both cytoplasmic and intranuclear inclusion bodies. MEASLES VIRUS is the type species. [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]

Morphogenesis: The development of the form of an organ, part of the body, or organism. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Morphology: The science of the form and structure of organisms (plants, animals, and other forms of life). [NIH]

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 Skills: Performance of complex motor acts. [NIH]

Mucins: A secretion containing mucopolysaccharides and protein that is the chief constituent of 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]

Muscarinic Agonists: Drugs that bind to and activate muscarinic cholinergic receptors (receptors, muscarinic). Muscarinic agonists are most commonly used when it is desirable to increase smooth muscle tone, especially in the GI tract, urinary bladder and the eye. They may also be used to reduce heart rate. [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 Spasticity: Strongly marked hypertonicity of muscles. [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]

Mutagenesis: Process of generating genetic mutations. It may occur spontaneously or be induced by mutagens. [NIH]

Mutagens: Chemical agents that increase the rate of genetic mutation by interfering with the function of nucleic acids. A clastogen is a specific mutagen that causes breaks in chromosomes. [NIH]

Mycophenolate mofetil: A drug that is being studied for its effectiveness in preventing graft-versus-host disease and autoimmune disorders. [NIH]

Myenteric: On stimulation of an intestinal segment, the segment above contracts and that below relaxes. [NIH]

Myocardial Ischemia: A disorder of cardiac function caused by insufficient blood flow to the muscle tissue of the heart. The decreased blood flow may be due to narrowing of the coronary arteries (coronary arteriosclerosis), to obstruction by a thrombus (coronary thrombosis), or less commonly, to diffuse narrowing of arterioles and other small vessels within the heart. Severe interruption of the blood supply to the myocardial tissue may result in necrosis of cardiac muscle (myocardial infarction). [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]

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]

Naive: Used to describe an individual who has never taken a certain drug or class of drugs (e. g., AZT-naive, antiretroviral-naive), or to refer to an undifferentiated immune system cell. [NIH]

Nalidixic Acid: Synthetic antimicrobial agent used in urinary tract infections. It is active against gram-negative bacteria but has little activity against gram-positive organisms or Pseudomonas. [NIH]

Naphazoline: An adrenergic vasoconstrictor agent used as a decongestant. [NIH]

Narcolepsy: A condition of unknown cause characterized by a periodic uncontrollable tendency to fall asleep. [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]

Nasogastric: The process of passing a small, flexible plastic tube through the nose or mouth into the stomach or small intestine. [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]

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]

Nelfinavir: A potent HIV protease inhibitor. It is used in combination with other antiviral drugs in the treatment of HIV in both adults and children. [NIH]

Neonatal: Pertaining to the first four weeks after birth. [EU]

Neonatal Abstinence Syndrome: Fetal and neonatal addiction and withdrawal as a result of the mother's dependence on drugs during pregnancy. Withdrawal or abstinence symptoms develop shortly after birth. Symptoms exhibited are loud, high-pitched crying, sweating, yawning and gastrointestinal disturbances. [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]

Nephrosis: Descriptive histopathologic term for renal disease without an inflammatory component. [NIH]

Nephrotic: Pertaining to, resembling, or caused by nephrosis. [EU]

Nephrotic Syndrome: Clinical association of heavy proteinuria, hypoalbuminemia, and generalized edema. [NIH]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

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

Networks: Pertaining to a nerve or to the nerves, a meshlike structure of interlocking fibers or strands. [NIH]

Neural: 1. Pertaining to a nerve or to the nerves. 2. Situated in the region of the spinal axis, as the neutral arch. [EU]

Neural Pathways: Neural tracts connecting one part of the nervous system with another. [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]

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]

Neurofibrillary Tangles: Abnormal structures located in various parts of the brain and composed of dense arrays of paired helical filaments (neurofilaments and microtubules). These double helical stacks of transverse subunits are twisted into left-handed ribbon-like

filaments that likely incorporate the following proteins: (1) the intermediate filaments: medium- and high-molecular-weight neurofilaments; (2) the microtubule-associated proteins map-2 and tau; (3) actin; and (4) ubiquitin. As one of the hallmarks of Alzheimer disease, the neurofibrillary tangles eventually occupy the whole of the cytoplasm in certain classes of cell in the neocortex, hippocampus, brain stem, and diencephalon. The number of these tangles, as seen in post mortem histology, correlates with the degree of dementia during life. Some studies suggest that tangle antigens leak into the systemic circulation both in the course of normal aging and in cases of Alzheimer disease. [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]

Neurologic: Having to do with nerves or the nervous system. [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]

Neurophysiology: The scientific discipline concerned with the physiology of the nervous system. [NIH]

Neuropil: A dense intricate feltwork of interwoven fine glial processes, fibrils, synaptic terminals, axons, and dendrites interspersed among the nerve cells in the gray matter of the central nervous system. [NIH]

Neuropil Threads: Abnormal structures located chiefly in distal dendrites and, along with neurofibrillary tangles and senile plaques, constitute the three morphological hallmarks of Alzheimer disease. Neuropil threads are made up of straight and paired helical filaments which consist of abnormally phosphorylated microtubule-associated tau proteins. It has been suggested that the threads have a major role in the cognitive impairment seen in Alzheimer disease. [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]

Neutralization: An act or process of neutralizing. [EU]

Neutrons: Electrically neutral elementary particles found in all atomic nuclei except light hydrogen; the mass is equal to that of the proton and electron combined and they are unstable when isolated from the nucleus, undergoing beta decay. Slow, thermal, epithermal, and fast neutrons refer to the energy levels with which the neutrons are ejected from heavier

nuclei during their decay. [NIH]

Neutropenia: An abnormal decrease in the number of neutrophils, a type of white blood cell. [NIH]

Neutrophil: A type of white blood cell. [NIH]

Neutrophil Infiltration: The diffusion or accumulation of neutrophils in tissues or cells in response to a wide variety of substances released at the sites of inflammatory reactions. [NIH]

Nevirapine: A potent, non-nucleoside reverse transcriptase inhibitor used in combination with nucleoside analogues for treatment of HIV infection and AIDS. [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]

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]

Nizatidine: A histamine H2 receptor antagonist with low toxicity that inhibits gastric acid secretion. The drug is used for the treatment of duodenal ulcers. [NIH]

Non-nucleoside: A member of a class of compounds, including delavirdine, loviride and nevirapine, that acts to directly combine with and block the action of HIV's reverse transcriptase. [NIH]

Nonverbal Communication: Transmission of emotions, ideas, and attitudes between individuals in ways other than the spoken language. [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]

Nosocomial: Pertaining to or originating in the hospital, said of an infection not present or incubating prior to admittance to the hospital, but generally occurring 72 hours after admittance; the term is usually used to refer to patient disease, but hospital personnel may also acquire nosocomial infection. [EU]

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]

Nuclear Proteins: Proteins found in the nucleus of a cell. Do not confuse with nucleoproteins which are proteins conjugated with nucleic acids, that are not necessarily present in the nucleus. [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]

Nucleocapsid: A protein-nucleic acid complex which forms part or all of a virion. It consists of a capsid plus enclosed nucleic acid. Depending on the virus, the nucleocapsid may correspond to a naked core or be surrounded by a membranous envelope. [NIH]

Nucleoli: A small dense body (sub organelle) within the nucleus of eukaryotic cells, visible by phase contrast and interference microscopy in live cells throughout interphase. Contains RNA and protein and is the site of synthesis of ribosomal RNA. [NIH]

Nucleoproteins: Proteins conjugated with nucleic acids. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nurseries: Facilities which provide care for infants. [NIH]

Nutritional Status: State of the body in relation to the consumption and utilization of nutrients. [NIH]

Nutritional Support: The administration of nutrients for assimilation and utilization by a patient by means other than normal eating. It does not include fluid therapy which normalizes body fluids to restore water-electrolyte balance. [NIH]

Occult: Obscure; concealed from observation, difficult to understand. [EU]

Occult Blood: Chemical, spectroscopic, or microscopic detection of extremely small amounts of blood. [NIH]

Octreotide: A potent, long-acting somatostatin octapeptide analog which has a wide range of physiological actions. It inhibits growth hormone secretion, is effective in the treatment of hormone-secreting tumors from various organs, and has beneficial effects in the management of many pathological states including diabetes mellitus, orthostatic hypertension, hyperinsulinism, hypergastrinemia, and small bowel fistula. [NIH]

Ocular: 1. Of, pertaining to, or affecting the eye. 2. Eyepiece. [EU]

Odour: A volatile emanation that is perceived by the sense of smell. [EU]

Odynophagia: A painful condition of the esophagus. [NIH]

Oedema: The presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body; usually applied to demonstrable accumulation of excessive fluid in the subcutaneous tissues. Edema may be localized, due to venous or lymphatic obstruction or to increased vascular permeability, or it may be systemic due to heart failure or renal disease. Collections of edema fluid are designated according to the site, e.g. ascites (peritoneal cavity), hydrothorax (pleural cavity), and hydropericardium (pericardial sac). Massive generalized edema is called anasarca. [EU]

Oligo: Chemical and mineral elements that exist in minimal (oligo) quantities in the body, in foods, in the air, in soil; name applied to any element observed as a microconstituent of plant or animal tissue and of beneficial, harmful, or even doubtful significance. [NIH]

Oligosaccharides: Carbohydrates consisting of between two and ten monosaccharides connected by either an alpha- or beta-glycosidic link. They are found throughout nature in both the free and bound form. [NIH]

Oliguria: Clinical manifestation of the urinary system consisting of a decrease in the amount of urine secreted. [NIH]

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]

Oncologist: A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment. For example, a radiation oncologist specializes in treating cancer with radiation. [NIH]

Oocytes: Female germ cells in stages between the prophase of the first maturation division and the completion of the second maturation division. [NIH]

Opacity: Degree of density (area most dense taken for reading). [NIH]

Open Reading Frames: Reading frames where successive nucleotide triplets can be read as codons specifying amino acids and where the sequence of these triplets is not interrupted by stop codons. [NIH]

Operon: The genetic unit consisting of a feedback system under the control of an operator gene, in which a structural gene transcribes its message in the form of mRNA upon blockade of a repressor produced by a regulator gene. Included here is the attenuator site of bacterial operons where transcription termination is regulated. [NIH]

Opioid Peptides: The endogenous peptides with opiate-like activity. The three major classes currently recognized are the enkephalins, the dynorphins, and the endorphins. Each of these families derives from different precursors, proenkephalin, prodynorphin, and pro-opiomelanocortin, respectively. There are also at least three classes of opioid receptors, but the peptide families do not map to the receptors in a simple way. [NIH]

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]

Orderly: A male hospital attendant. [NIH]

Organ Culture: The growth in aseptic culture of plant organs such as roots or shoots, beginning with organ primordia or segments and maintaining the characteristics of the organ. [NIH]

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]

Orthostatic: Pertaining to or caused by standing erect. [EU]

Osmolality: The concentration of osmotically active particles in solution expressed in terms of osmoles of solute per kilogram of solvent. The osmolality is directly proportional to the colligative properties of solutions; osmotic pressure, boiling point elevation, freezing point depression, and vapour pressure lowering. [EU]

Osmolarity: The concentration of osmotically active particles expressed in terms of osmoles of solute per litre of solution. [EU]

Osmoles: The standard unit of osmotic pressure. [NIH]

Osmosis: Tendency of fluids (e.g., water) to move from the less concentrated to the more concentrated side of a semipermeable membrane. [NIH]

Osmotic: Pertaining to or of the nature of osmosis (= the passage of pure solvent from a solution of lesser to one of greater solute concentration when the two solutions are separated by a membrane which selectively prevents the passage of solute molecules, but is permeable to the solvent). [EU]

Osteoarthritis: A progressive, degenerative joint disease, the most common form of arthritis, especially in older persons. The disease is thought to result not from the aging process but from biochemical changes and biomechanical stresses affecting articular cartilage. In the foreign literature it is often called osteoarthrosis deformans. [NIH]

Osteonecrosis: Death of a bone or part of a bone, either atraumatic or posttraumatic. [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]

Ostomy: Surgical construction of an artificial opening (stoma) for external fistulization of a duct or vessel by insertion of a tube with or without a supportive stent. [NIH]

Otitis: Inflammation of the ear, which may be marked by pain, fever, abnormalities of hearing, hearing loss, tinnitus, and vertigo. [EU]

Otitis Media: Inflammation of the middle ear. [NIH]

Overdose: An accidental or deliberate dose of a medication or street drug that is in excess of what is normally used. [NIH]

Overweight: An excess of body weight but not necessarily body fat; a body mass index of 25 to 29.9 kg/m2. [NIH]

Ovum: A female germ cell extruded from the ovary at ovulation. [NIH]

Oxalate: A chemical that combines with calcium in urine to form the most common type of kidney stone (calcium oxalate stone). [NIH]

Oxidative metabolism: A chemical process in which oxygen is used to make energy from carbohydrates (sugars). Also known as aerobic respiration, cell respiration, or aerobic metabolism. [NIH]

Oxygen Consumption: The oxygen consumption is determined by calculating the difference between the amount of oxygen inhaled and exhaled. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

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 enzymes: A group of proteins secreted by the pancreas which aid in the digestion of food. [NIH]

Pancreatic Insufficiency: Absence of or reduced pancreatic exocrine secretion into the duodenum and resultant poor digestion of lipids, vitamins, nitrogen, and carbohydrates. [NIH]

Pancreatic Juice: The fluid containing digestive enzymes secreted by the pancreas in response to food in the duodenum. [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]

Pancrelipase: A preparation of hog pancreatic enzymes standardized for lipase content. [NIH]

Pancytopenia: Deficiency of all three cell elements of the blood, erythrocytes, leukocytes and platelets. [NIH]

Paneth Cells: Epithelial cells found in the basal part of the intestinal glands (crypts of Lieberkuhn). Paneth cells synthesize and secrete lysozyme and cryptdins. [NIH]

Panic: A state of extreme acute, intense anxiety and unreasoning fear accompanied by disorganization of personality function. [NIH]

Papaverine: An alkaloid found in opium but not closely related to the other opium alkaloids in its structure or pharmacological actions. It is a direct-acting smooth muscle relaxant used in the treatment of impotence and as a vasodilator, especially for cerebral vasodilation. The mechanism of its pharmacological actions is not clear, but it apparently can inhibit phosphodiesterases and it may have direct actions on calcium channels. [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]

Parasitic: Having to do with or being a parasite. A parasite is an animal or a plant that lives on or in an organism of another species and gets at least some of its nutrients from it. [NIH]

Parasitic Diseases: Infections or infestations with parasitic organisms. They are often contracted through contact with an intermediate vector, but may occur as the result of direct exposure. [NIH]

Parenteral: Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, etc. [EU]

Parotid: The space that contains the parotid gland, the facial nerve, the external carotid artery, and the retromandibular vein. [NIH]

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]

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]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

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]

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]

Pepsin A: Formed from pig pepsinogen by cleavage of one peptide bond. The enzyme is a single polypeptide chain and is inhibited by methyl 2-diaazoacetamidohexanoate. It cleaves peptides preferentially at the carbonyl linkages of phenylalanine or leucine and acts as the principal digestive enzyme of gastric juice. [NIH]

Peptic: Pertaining to pepsin or to digestion; related to the action of gastric juices. [EU]

Peptic Ulcer: Ulcer that occurs in those portions of the alimentary tract which come into contact with gastric juice containing pepsin and acid. It occurs when the amount of acid and pepsin is sufficient to overcome the gastric mucosal barrier. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Peptide Elongation Factors: Protein factors uniquely required during the elongation phase of protein synthesis. [NIH]

Peptide T: N-(N-(N(2)-(N-(N-(N-(N-D-Alanyl L-seryl)-L-threonyl)-L-threonyl) L-threonyl)-L-asparaginyl)-L-tyrosyl) L-threonine. Octapeptide sharing sequence homology with HIV envelope protein gp120. It is potentially useful as antiviral agent in AIDS therapy. The core pentapeptide sequence, TTNYT, consisting of amino acids 4-8 in peptide T, is the HIV envelope sequence required for attachment to the CD4 receptor. [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]

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]

Perianal: Located around the anus. [EU]

Perineum: The area between the anus and the sex organs. [NIH]

Peripheral blood: Blood circulating throughout the body. [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]

Peritoneal: Having to do with the peritoneum (the tissue that lines the abdominal wall and

covers most of the organs in the abdomen). [NIH]

Peritoneal Cavity: The space enclosed by the peritoneum. It is divided into two portions, the greater sac and the lesser sac or omental bursa, which lies behind the stomach. The two sacs are connected by the foramen of Winslow, or epiploic foramen. [NIH]

Peritoneum: Endothelial lining of the abdominal cavity, the parietal peritoneum covering the inside of the abdominal wall and the visceral peritoneum covering the bowel, the mesentery, and certain of the organs. The portion that covers the bowel becomes the serosal layer of the bowel wall. [NIH]

Peritonitis: Inflammation of the peritoneum; a condition marked by exudations in the peritoneum of serum, fibrin, cells, and pus. It is attended by abdominal pain and tenderness, constipation, vomiting, and moderate fever. [EU]

Perspiration: Sweating; the functional secretion of sweat. [EU]

Pestivirus: A genus of Flaviviridae, also known as mucosal disease virus group, which is not arthropod-borne. Transmission is by direct and indirect contact, and by transplacental and congenital transmission. Species include border disease virus, bovine viral diarrhea virus, and hog cholera virus. [NIH]

PH: The symbol relating the hydrogen ion (H+) concentration or activity of a solution to that of a given standard solution. Numerically the pH is approximately equal to the negative logarithm of H+ concentration expressed in molarity. pH 7 is neutral; above it alkalinity increases and below it acidity increases. [EU]

Phagocytosis: The engulfing of microorganisms, other cells, and foreign particles by phagocytic cells. [NIH]

Pharmaceutical Preparations: Drugs intended for human or veterinary use, presented in their finished dosage form. Included here are materials used in the preparation and/or formulation of the finished dosage form. [NIH]

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]

Pharmacopoeias: Authoritative treatises on drugs and preparations, their description, formulation, analytic composition, physical constants, main chemical properties used in identification, standards for strength, purity, and dosage, chemical tests for determining identity and purity, etc. They are usually published under governmental jurisdiction (e.g., USP, the United States Pharmacopoeia; BP, British Pharmacopoeia; P. Helv., the Swiss Pharmacopoeia). They differ from formularies in that they are far more complete: formularies tend to be mere listings of formulas and prescriptions. [NIH]

Pharynx: The hollow tube about 5 inches long that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes to the stomach). [NIH]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of yeasts. [NIH]

Phenoxybenzamine: An alpha-adrenergic anatagonist with long duration of action. It has been used to treat hypertension and as a peripheral vasodilator. [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]

Phospholipases: A class of enzymes that catalyze the hydrolysis of phosphoglycerides or glycerophosphatidates. EC 3.1.-. [NIH]

Phospholipids: Lipids containing one or more phosphate groups, particularly those derived from either glycerol (phosphoglycerides; glycerophospholipids) or sphingosine (sphingolipids). They are polar lipids that are of great importance for the structure and function of cell membranes and are the most abundant of membrane lipids, although not stored in large amounts in the system. [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]

Photocoagulation: Using a special strong beam of light (laser) to seal off bleeding blood vessels such as in the eye. The laser can also burn away blood vessels that should not have grown in the eye. This is the main treatment for diabetic retinopathy. [NIH]

Physical Examination: Systematic and thorough inspection of the patient for physical signs of disease or abnormality. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Physiology: The science that deals with the life processes and functions of organismus, their cells, tissues, and organs. [NIH]

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]

Pirenzepine: An antimuscarinic agent that inhibits gastric secretion at lower doses than are required to affect gastrointestinal motility, salivary, central nervous system, cardiovascular, ocular, and urinary function. It promotes the healing of duodenal ulcers and due to its cytoprotective action is beneficial in the prevention of duodenal ulcer recurrence. It also potentiates the effect of other antiulcer agents such as cimetidine and ranitidine. It is generally well tolerated by patients. [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]

Plague: An acute infectious disease caused by Yersinia pestis that affects humans, wild rodents, and their ectoparasites. This condition persists due to its firm entrenchment in sylvatic rodent-flea ecosystems throughout the world. Bubonic plague is the most common form. [NIH]

Plana: The radiographic term applied to a vertebral body crushed to a thin plate. [NIH]

Plant Diseases: Diseases of plants. [NIH]

Plants: Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized

by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

Plaque: A clear zone in a bacterial culture grown on an agar plate caused by localized destruction of bacterial cells by a bacteriophage. The concentration of infective virus in a fluid can be estimated by applying the fluid to a culture and counting the number of. [NIH]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

Plasma Kallikrein: A peptidohydrolytic enzyme that is formed from prekallikrein by factor XIIA. It activates factor XII, factor VII, and plasminogen. It is selective for both arginine and to a lesser extent lysinebonds. EC 3.4.21.34. [NIH]

Plasmid: An autonomously replicating, extra-chromosomal DNA molecule found in many bacteria. Plasmids are widely used as carriers of cloned genes. [NIH]

Plasmin: A product of the lysis of plasminogen (profibrinolysin) by plasminogen activators. It is composed of two polypeptide chains, light (B) and heavy (A), with a molecular weight of 75,000. It is the major proteolytic enzyme involved in blood clot retraction or the lysis of fibrin and quickly inactivated by antiplasmins. EC 3.4.21.7. [NIH]

Plasminogen: Precursor of fibrinolysin (plasmin). It is a single-chain beta-globulin of molecular weight 80-90,000 found mostly in association with fibrinogen in plasma; plasminogen activators change it to fibrinolysin. It is used in wound debriding and has been investigated as a thrombolytic agent. [NIH]

Plasminogen Activators: A heterogeneous group of proteolytic enzymes that convert plasminogen to plasmin. They are concentrated in the lysosomes of most cells and in the vascular endothelium, particularly in the vessels of the microcirculation. EC 3.4.21.-. [NIH]

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]

Platelet Factor 4: A high-molecular-weight proteoglycan-platelet factor complex which is released from blood platelets by thrombin. It acts as a mediator in the heparin-neutralizing capacity of the blood and plays a role in platelet aggregation. At high ionic strength (I=0.75), the complex dissociates into the active component (molecular weight 29,000) and the proteoglycan carrier (chondroitin 4-sulfate, molecular weight 350,000). The molecule exists in the form of a dimer consisting of 8 moles of platelet factor 4 and 2 moles of proteoglycan. [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]

Pleural: A circumscribed area of hyaline whorled fibrous tissue which appears on the

surface of the parietal pleura, on the fibrous part of the diaphragm or on the pleura in the interlobar fissures. [NIH]

Pleural cavity: A space enclosed by the pleura (thin tissue covering the lungs and lining the interior wall of the chest cavity). It is bound by thin membranes. [NIH]

Plexus: A network or tangle; a general term for a network of lymphatic vessels, nerves, or veins. [EU]

Point Mutation: A mutation caused by the substitution of one nucleotide for another. This results in the DNA molecule having a change in a single base pair. [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]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand as a template. The polymerase copies the template in the 5'-3'direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

Polymerase Chain Reaction: In vitro method for producing large amounts of specific DNA or RNA fragments of defined length and sequence from small amounts of short oligonucleotide flanking sequences (primers). The essential steps include thermal denaturation of the double-stranded target molecules, annealing of the primers to their complementary sequences, and extension of the annealed primers by enzymatic synthesis with DNA polymerase. The reaction is efficient, specific, and extremely sensitive. Uses for the reaction include disease diagnosis, detection of difficult-to-isolate pathogens, mutation analysis, genetic testing, DNA sequencing, and analyzing evolutionary relationships. [NIH]

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Polyposis: The development of numerous polyps (growths that protrude from a mucous membrane). [NIH]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Posterior: Situated in back of, or in the back part of, or affecting the back or dorsal surface of the body. In lower animals, it refers to the caudal end of the body. [EU]

Postmenopausal: Refers to the time after menopause. Menopause is the time in a woman's life when menstrual periods stop permanently; also called "change of life." [NIH]

Postoperative: After surgery. [NIH]

Postprandial: Occurring after dinner, or after a meal; postcibal. [EU]

Postsynaptic: Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

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]

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]

Prazosin: A selective adrenergic alpha-1 antagonist used in the treatment of heart failure, hypertension, pheochromocytoma, Raynaud's syndrome, prostatic hypertrophy, and urinary retention. [NIH]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Prekallikrein: A plasma protein which is the precursor of kallikrein. Plasma that is deficient in prekallikrein has been found to be abnormal in thromboplastin formation, kinin generation, evolution of a permeability globulin, and plasmin formation. The absence of prekallikrein in plasma leads to Fletcher factor deficiency, a congenital disease. [NIH]

Premedication: Preliminary administration of a drug preceding a diagnostic, therapeutic, or surgical procedure. The commonest types of premedication are antibiotics (antibiotic prophylaxis) and anti-anxiety agents. It does not include preanesthetic medication. [NIH]

Presbyopia: The normal decreasing elasticity of the crystalline lens that leads to loss of accommodation. [NIH]

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

Presynaptic: Situated proximal to a synapse, or occurring before the synapse is crossed. [EU]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Progeny: The offspring produced in any generation. [NIH]

Proglumide: 4-Benzamido-N,N-dipropylglutaramic acid. A drug that exerts an inhibitory effect on gastric secretion and reduces gastrointestinal motility. It is used clinically in the drug therapy of gastrointestinal ulcers. [NIH]

Prognostic factor: A situation or condition, or a characteristic of a patient, that can be used to estimate the chance of recovery from a disease, or the chance of the disease recurring (coming back). [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]

Progressive disease: Cancer that is increasing in scope or severity. [NIH]

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]

Promoter: A chemical substance that increases the activity of a carcinogenic process. [NIH]

Promotor: In an operon, a nucleotide sequence located at the operator end which contains all the signals for the correct initiation of genetic transcription by the RNA polymerase holoenzyme and determines the maximal rate of RNA synthesis. [NIH]

Prone: Having the front portion of the body downwards. [NIH]

Pro-Opiomelanocortin: A precursor protein, MW 30,000, synthesized mainly in the anterior pituitary gland but also found in the hypothalamus, brain, and several peripheral tissues. It incorporates the amino acid sequences of ACTH and beta-lipotropin. These two hormones, in turn, contain the biologically active peptides MSH, corticotropin-like intermediate lobe peptide, alpha-lipotropin, endorphins, and methionine enkephalin. [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]

Propiolactone: Disinfectant used in vapor form to sterilize vaccines, grafts, etc. The vapor is very irritating and the liquid form is carcinogenic. [NIH]

Proportional: Being in proportion : corresponding in size, degree, or intensity, having the same or a constant ratio; of, relating to, or used in determining proportions. [EU]

Propulsive: Tending or having power to propel; driving onward or forward; impelling to action or motion. [EU]

Prospective study: An epidemiologic study in which a group of individuals (a cohort), all free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

Prostaglandin: Any of a group of components derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway that are extremely potent mediators of a diverse group of physiologic processes. The abbreviation for prostaglandin is PG; specific compounds are designated by adding one of the letters A through I to indicate the type of substituents found on the hydrocarbon skeleton and a subscript (1, 2 or 3) to indicate the number of double bonds in the hydrocarbon skeleton e.g., PGE2. The predominant naturally occurring prostaglandins all have two double bonds and are synthesized from arachidonic acid (5,8,11,14-eicosatetraenoic acid) by the pathway shown in the illustration. The 1 series and 3 series are produced by the same pathway with fatty acids having one fewer double bond (8,11,14-eicosatrienoic acid or one more double bond (5,8,11,14,17-eicosapentaenoic acid) than arachidonic acid. The subscript a or ß indicates the configuration at C-9 (a denotes a substituent below the plane of the ring, ß, above the plane). The naturally occurring PGF's have the a configuration, e.g., PGF2a. All of the prostaglandins act by binding to specific cell-surface receptors causing an increase in the level of the intracellular second messenger cyclic AMP (and in some cases cyclic GMP also). The effect produced by the cyclic AMP increase depends on the specific cell type. In some cases there is also a positive feedback effect. Increased cyclic AMP increases prostaglandin synthesis leading to further increases in cyclic AMP. [EU]

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]

Prostaglandins D: Physiologically active prostaglandins found in many tissues and organs. They show pressor activity, are mediators of inflammation, and have potential antithrombotic effects. [NIH]

Prostate: A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

Protease Inhibitors: Compounds which inhibit or antagonize biosynthesis or actions of proteases (endopeptidases). [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 Binding: The process in which substances, either endogenous or exogenous, bind to proteins, peptides, enzymes, protein precursors, or allied compounds. Specific protein-binding measures are often used as assays in diagnostic assessments. [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 Kinase C: An enzyme that phosphorylates proteins on serine or threonine residues in the presence of physiological concentrations of calcium and membrane phospholipids. The additional presence of diacylglycerols markedly increases its sensitivity to both calcium and phospholipids. The sensitivity of the enzyme can also be increased by phorbol esters and it is believed that protein kinase C is the receptor protein of tumor-promoting phorbol esters. EC 2.7.1.-. [NIH]

Protein Kinases: A family of enzymes that catalyze the conversion of ATP and a protein to ADP and a phosphoprotein. EC 2.7.1.37. [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]

Protein Transport: The process of moving proteins from one cellular compartment (including extracellular) to another by various sorting and transport mechanisms such as gated transport, protein translocation, and vesicular transport. [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]

Protein-Serine-Threonine Kinases: A group of enzymes that catalyzes the phosphorylation of serine or threonine residues in proteins, with ATP or other nucleotides as phosphate donors. EC 2.7.10. [NIH]

Proteinuria: The presence of protein in the urine, indicating that the kidneys are not working properly. [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]

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]

Proton Pump: Integral membrane proteins that transport protons across a membrane against a concentration gradient. This transport is driven by hydrolysis of ATP by H(+)-transporting ATP synthase. [NIH]

Proton Pump Inhibitors: Medicines that stop the stomach's acid pump. Examples are omeprazole (oh-MEH-prah-zol) (Prilosec) and lansoprazole (lan-SOH-prah-zol) (Prevacid). [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]

Protozoal: Having to do with the simplest organisms in the animal kingdom. Protozoa are single-cell organisms, such as ameba, and are different from bacteria, which are not members of the animal kingdom. Some protozoa can be seen without a microscope. [NIH]

Proximal: Nearest; closer to any point of reference; opposed to distal. [EU]

Pruritic: Pertaining to or characterized by pruritus. [EU]

Pruritus: An intense itching sensation that produces the urge to rub or scratch the skin to obtain relief. [NIH]

Pseudomembranous Colitis: Severe irritation of the colon. Caused by Clostridium difficile bacteria. Occurs after taking oral antibiotics, which kill bacteria that normally live in the colon. [NIH]

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]

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]

Psyllium: Dried, ripe seeds of Plantago psyllium, P. indica, and P. ovata (Plantaginaceae). Plantain seeds swell in water and are used as demulcents and bulk laxatives. [NIH]

Public Facilities: An area of recreation or hygiene for use by the public. [NIH]

Public Health: Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the international, national, state, or municipal level. [NIH]

Public 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 Emphysema: Condition of the lungs characterized by increase beyond normal in the size of air spaces distal to the terminal bronchioles, either from dilatation of the alveoli or from destruction of their walls. [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]

Purgative: 1. Cathartic (def. 1); causing evacuation of the bowels. 2. A cathartic, particularly one that stimulates peristaltic action. [EU]

Purines: A series of heterocyclic compounds that are variously substituted in nature and are known also as purine bases. They include adenine and guanine, constituents of nucleic acids, as well as many alkaloids such as caffeine and theophylline. Uric acid is the metabolic end product of purine metabolism. [NIH]

Purpura: Purplish or brownish red discoloration, easily visible through the epidermis, caused by hemorrhage into the tissues. [NIH]

Purulent: Consisting of or containing pus; associated with the formation of or caused by pus. [EU]

Pylorus: The opening in a vertebrate from the stomach into the intestine. [EU]

Pyramidal Tracts: Fibers that arise from cells within the cerebral cortex, pass through the medullary pyramid, and descend in the spinal cord. Many authorities say the pyramidal tracts include both the corticospinal and corticobulbar tracts. [NIH]

Quality of Life: A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

Quiescent: Marked by a state of inactivity or repose. [EU]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

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]

Radiolabeled: Any compound that has been joined with a radioactive substance. [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]

Raffinose: A trisaccharide occurring in Australian manna (from Eucalyptus spp, Myrtaceae) and in cottonseed meal. [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]

Ranitidine: A non-imidazole blocker of those histamine receptors that mediate gastric secretion (H2 receptors). It is used to treat gastrointestinal ulcers. [NIH]

Reabsorption: 1. The act or process of absorbing again, as the selective absorption by the kidneys of substances (glucose, proteins, sodium, etc.) already secreted into the renal tubules, and their return to the circulating blood. 2. Resorption. [EU]

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]

Reassurance: A procedure in psychotherapy that seeks to give the client confidence in a favorable outcome. It makes use of suggestion, of the prestige of the therapist. [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, Adrenergic: Cell-surface proteins that bind epinephrine and/or norepinephrine with high affinity and trigger intracellular changes. The two major classes of adrenergic receptors, alpha and beta, were originally discriminated based on their cellular actions but now are distinguished by their relative affinity for characteristic synthetic ligands. Adrenergic receptors may also be classified according to the subtypes of G-proteins with which they bind; this scheme does not respect the alpha-beta distinction. [NIH]

Receptors, Muscarinic: One of the two major classes of cholinergic receptors. Muscarinic receptors were originally defined by their preference for muscarine over nicotine. There are several subtypes (usually M1, M2, M3.) that are characterized by their cellular actions, pharmacology, and molecular biology. [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]

Recombination: The formation of new combinations of genes as a result of segregation in crosses between genetically different parents; also the rearrangement of linked genes due to crossing-over. [NIH]

Reconstitution: 1. A type of regeneration in which a new organ forms by the rearrangement of tissues rather than from new formation at an injured surface. 2. The restoration to original form of a substance previously altered for preservation and storage, as the restoration to a liquid state of blood serum or plasma that has been dried and stored. [EU]

Rectal: By or having to do with the rectum. The rectum is the last 8 to 10 inches of the large intestine and ends at the anus. [NIH]

Rectum: The last 8 to 10 inches of the large intestine. [NIH]

Recurrence: The return of a sign, symptom, or disease after a remission. [NIH]

Red blood cells: RBCs. Cells that carry oxygen to all parts of the body. Also called erythrocytes. [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]

Reflective: Capable of throwing back light, images, sound waves : reflecting. [EU]

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]

Refractory: Not readily yielding to treatment. [EU]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Regurgitation: A backward flowing, as the casting up of undigested food, or the backward flowing of blood into the heart, or between the chambers of the heart when a valve is incompetent. [EU]

Rehydration: The restoration of water or of fluid content to a body or to substance which has become dehydrated. [EU]

Rehydration Solutions: Fluids restored to the body in order to maintain normal water-electrolyte balance. [NIH]

Relapse: The return of signs and symptoms of cancer after a period of improvement. [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 failure: Progressive renal insufficiency and uremia, due to irreversible and progressive renal glomerular tubular or interstitial disease. [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]

Resected: Surgical removal of part of an organ. [NIH]

Resection: Removal of tissue or part or all of an organ by surgery. [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]

Respirator: A mechanical device that helps a patient breathe; a mechanical ventilator. [NIH]

Respiratory syncytial virus: RSV. A virus that causes respiratory infections with cold-like symptoms. [NIH]

Response rate: The percentage of patients whose cancer shrinks or disappears after treatment. [NIH]

Restitution: The restoration to a normal state. [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]

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]

Retrograde: 1. Moving backward or against the usual direction of flow. 2. Degenerating, deteriorating, or catabolic. [EU]

Reverse Transcriptase Inhibitors: Inhibitors of reverse transcriptase (RNA-directed DNA polymerase), an enzyme that synthesizes DNA on an RNA template. [NIH]

Reversion: A return to the original condition, e. g. the reappearance of the normal or wild type in previously mutated cells, tissues, or organisms. [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]

Ribose: A pentose active in biological systems usually in its D-form. [NIH]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Ristocetin: An antibiotic mixture of two components, A and B, obtained from Nocardia lurida (or the same substance produced by any other means). It is no longer used clinically because of its toxicity. It causes platelet agglutination and blood coagulation and is used to assay those functions in vitro. [NIH]

Ritonavir: An HIV protease inhibitor that works by interfering with the reproductive cycle of HIV. [NIH]

Rod: A reception for vision, located in the retina. [NIH]

Rotavirus: A genus of Reoviridae, causing acute gastroenteritis in birds and mammals, including humans. Transmission is horizontal and by environmental contamination. [NIH]

Rotavirus Infections: Infection with any of the rotaviruses. Specific infections include human infantile diarrhea, neonatal calf diarrhea, and epidemic diarrhea of infant mice. [NIH]

Rotavirus Vaccines: Vaccines or candidate vaccines used to prevent infection with rotavirus. [NIH]

Ryanodine: Insecticidal alkaloid isolated from Ryania speciosa; proposed as a myocardial depressant. [NIH]

Saline: A solution of salt and water. [NIH]

Saliva: The clear, viscous fluid secreted by the salivary glands and mucous glands of the mouth. It contains mucins, water, organic salts, and ptylin. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Salivation: 1. The secretion of saliva. 2. Ptyalism (= excessive flow of saliva). [EU]

Salmonella: A genus of gram-negative, facultatively anaerobic, rod-shaped bacteria that utilizes citrate as a sole carbon source. It is pathogenic for humans, causing enteric fevers, gastroenteritis, and bacteremia. Food poisoning is the most common clinical manifestation. Organisms within this genus are separated on the basis of antigenic characteristics, sugar fermentation patterns, and bacteriophage susceptibility. [NIH]

Salmonellosis: Infection by salmonellae. [NIH]

Sanitary: Relating or belonging to health and hygiene; conductive to the restoration or maintenance of health. [NIH]

Sanitation: The development and establishment of environmental conditions favorable to the health of the public. [NIH]

Saquinavir: An HIV protease inhibitor which acts as an analog of an HIV protease cleavage site. It is a highly specific inhibitor of HIV-1 and HIV-2 proteases. [NIH]

Sarcoidosis: An idiopathic systemic inflammatory granulomatous disorder comprised of epithelioid and multinucleated giant cells with little necrosis. It usually invades the lungs with fibrosis and may also involve lymph nodes, skin, liver, spleen, eyes, phalangeal bones, and parotid glands. [NIH]

Sarcoma: A connective tissue neoplasm formed by proliferation of mesodermal cells; it is usually highly malignant. [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]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Sebaceous: 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]

Secretin: A hormone made in the duodenum. Causes the stomach to make pepsin, the liver to make bile, and the pancreas to make a digestive juice. [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]

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]

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]

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]

Senna: Preparations of Cassia senna L. and C. angustifolia of the Leguminosae. They contain sennosides, which are anthraquinone type cathartics and are used in many different preparations as laxatives. [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]

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]

Sepsis: The presence of bacteria in the bloodstream. [NIH]

Septal: An abscess occurring at the root of the tooth on the proximal surface. [NIH]

Septal Nuclei: Neural nuclei situated in the septal region. They have afferent and cholinergic efferent connections with a variety of forebrain and brainstem areas including the hippocampus, the lateral hypothalamus, the tegmentum, and the amygdala. Included are the dorsal, lateral, medial, and triangular septal nuclei, septofimbrial nucleus, nucleus of diagonal band, nucleus of anterior commissure, and the nucleus of stria terminalis. [NIH]

Septicaemia: A term originally used to denote a putrefactive process in the body, but now usually referring to infection with pyogenic micro-organisms; a genus of Diptera; the severe type of infection in which the blood stream is invaded by large numbers of the causal. [NIH]

Sequence Homology: The degree of similarity between sequences. Studies of amino acid

and nucleotide sequences provide useful information about the genetic relatedness of certain species. [NIH]

Sequencing: The determination of the order of nucleotides in a DNA or RNA chain. [NIH]

Sequester: A portion of dead bone which has become detached from the healthy bone tissue, as occurs in necrosis. [NIH]

Serine: A non-essential amino acid occurring in natural form as the L-isomer. It is synthesized from glycine or threonine. It is involved in the biosynthesis of purines, pyrimidines, and other amino acids. [NIH]

Serologic: Analysis of a person's serum, especially specific immune or lytic serums. [NIH]

Serologic Tests: Diagnostic procedures involving immunoglobulin reactions. [NIH]

Serotonin: A biochemical messenger and regulator, synthesized from the essential amino acid L-tryptophan. In humans it is found primarily in the central nervous system, gastrointestinal tract, and blood platelets. Serotonin mediates several important physiological functions including neurotransmission, gastrointestinal motility, hemostasis, and cardiovascular integrity. Multiple receptor families (receptors, serotonin) explain the broad physiological actions and distribution of this biochemical mediator. [NIH]

Serotypes: A cause of haemorrhagic septicaemia (in cattle, sheep and pigs), fowl cholera of birds, pasteurellosis of rabbits, and gangrenous mastitis of ewes. It is also commonly found in atrophic rhinitis of pigs. [NIH]

Serous: Having to do with serum, the clear liquid part of blood. [NIH]

Serrata: The serrated anterior border of the retina located approximately 8.5 mm from the limbus and adjacent to the pars plana of the ciliary body. [NIH]

Serrated: Having notches or teeth on the edge as a saw has. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Sex Determination: The biological characteristics which distinguish human beings as female or male. [NIH]

Shedding: Release of infectious particles (e. g., bacteria, viruses) into the environment, for example by sneezing, by fecal excretion, or from an open lesion. [NIH]

Shiga Toxin: A toxin produced by Shigella dysenteriae. It is the protype of class of toxins that inhibit protein synthesis by blocking the interaction of ribosomal RNA with peptide elongation factors. [NIH]

Shigella: A genus of gram-negative, facultatively anaerobic, rod-shaped bacteria that ferments sugar without gas production. Its organisms are intestinal pathogens of man and other primates and cause bacillary dysentery. [NIH]

Shigellosis: Infection with the bacterium Shigella. Usually causes a high fever, acute diarrhea, and dehydration. [NIH]

Ships: Large vessels propelled by power or sail used for transportation on rivers, seas, oceans, or other navigable waters. Boats are smaller vessels propelled by oars, paddles, sail, or power; they may or may not have a deck. [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]

Short Bowel Syndrome: A malabsorption syndrome resulting from extensive operative resection of small bowel. [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]

Sigmoid: 1. Shaped like the letter S or the letter C. 2. The sigmoid colon. [EU]

Sigmoid Colon: The lower part of the colon that empties into the rectum. [NIH]

Sigmoidoscopy: Endoscopic examination, therapy or surgery of the sigmoid flexure. [NIH]

Signal Transduction: The intercellular or intracellular transfer of information (biological activation/inhibition) through a signal pathway. In each signal transduction system, an activation/inhibition signal from a biologically active molecule (hormone, neurotransmitter) is mediated via the coupling of a receptor/enzyme to a second messenger system or to an ion channel. Signal transduction plays an important role in activating cellular functions, cell differentiation, and cell proliferation. Examples of signal transduction systems are the GABA-postsynaptic receptor-calcium ion channel system, the receptor-mediated T-cell activation pathway, and the receptor-mediated activation of phospholipases. Those coupled to membrane depolarization or intracellular release of calcium include the receptor-mediated activation of cytotoxic functions in granulocytes and the synaptic potentiation of protein kinase activation. Some signal transduction pathways may be part of larger signal transduction pathways; for example, protein kinase activation is part of the platelet activation signal pathway. [NIH]

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]

Small cell lung cancer: A type of lung cancer in which the cells appear small and round when viewed under the microscope. Also called oat cell lung cancer. [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]

Sneezing: Sudden, forceful, involuntary expulsion of air from the nose and mouth caused by irritation to the mucous membranes of the upper respiratory tract. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

Sodium: An element that is a member of the alkali group of metals. It has the atomic symbol Na, atomic number 11, and atomic weight 23. With a valence of 1, it has a strong affinity for oxygen and other nonmetallic elements. Sodium provides the chief cation of the extracellular body fluids. Its salts are the most widely used in medicine. (From Dorland, 27th ed) Physiologically the sodium ion plays a major role in blood pressure regulation, maintenance of fluid volume, and electrolyte balance. [NIH]

Sodium Bicarbonate: A white, crystalline powder that is commonly used as a pH buffering agent, an electrolyte replenisher, systemic alkalizer and in topical cleansing solutions. [NIH]

Soft tissue: Refers to muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body. [NIH]

Solid tumor: Cancer of body tissues other than blood, bone marrow, or the lymphatic system. [NIH]

Solitary Nucleus: Gray matter located in the dorsomedial part of the medulla oblongata associated with the solitary tract. The solitary nucleus receives inputs from most organ systems including the terminations of the facial, glossopharyngeal, and vagus nerves. It is a major coordinator of autonomic nervous system regulation of cardiovascular, respiratory, gustatory, gastrointestinal, and chemoreceptive aspects of homeostasis. The solitary nucleus is also notable for the large number of neurotransmitters which are found therein. [NIH]

Solvent: 1. Dissolving; effecting a solution. 2. A liquid that dissolves or that is capable of dissolving; the component of a solution that is present in greater amount. [EU]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Somatic cells: All the body cells except the reproductive (germ) cells. [NIH]

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]

Sound wave: An alteration of properties of an elastic medium, such as pressure, particle displacement, or density, that propagates through the medium, or a superposition of such alterations. [NIH]

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]

Sperm: The fecundating fluid of the male. [NIH]

Sphincter: A ringlike band of muscle fibres that constricts a passage or closes a natural orifice; called also musculus sphincter. [EU]

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 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]

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]

Splenomegaly: Enlargement of the spleen. [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]

Sprue: A non febrile tropical disease of uncertain origin. [NIH]

Stabilization: The creation of a stable state. [EU]

Standard therapy: A currently accepted and widely used treatment for a certain type of cancer, based on the results of past research. [NIH]

Steatorrhea: A condition in which the body cannot absorb fat. Causes a buildup of fat in the stool and loose, greasy, and foul bowel movements. [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]

Stem Cells: Relatively undifferentiated cells of the same lineage (family type) that retain the ability to divide and cycle throughout postnatal life to provide cells that can become specialized and take the place of those that die or are lost. [NIH]

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]

Steroids: Drugs used to relieve swelling and inflammation. [NIH]

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]

Strand: DNA normally exists in the bacterial nucleus in a helix, in which two strands are coiled together. [NIH]

Stress: Forcibly exerted influence; pressure. Any condition or situation that causes strain or tension. Stress may be either physical or psychologic, or both. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

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]

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]

Subiculum: A region of the hippocampus that projects to other areas of the brain. [NIH]

Submucous: Occurring beneath the mucosa or a mucous membrane. [NIH]

Subspecies: A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

Substance P: An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

Substrate Specificity: A characteristic feature of enzyme activity in relation to the kind of substrate on which the enzyme or catalytic molecule reacts. [NIH]

Sucralfate: A basic aluminum complex of sulfated sucrose. It is advocated in the therapy of peptic, duodenal, and prepyloric ulcers, gastritis, reflux esophagitis, and other gastrointestinal irritations. It acts primarily at the ulcer site, where it has cytoprotective, pepsinostatic, antacid, and bile acid-binding properties. The drug is only slightly absorbed by the digestive mucosa, which explains the absence of systemic effects and toxicity. [NIH]

Suction: The removal of secretions, gas or fluid from hollow or tubular organs or cavities by means of a tube and a device that acts on negative pressure. [NIH]

Superinfection: A frequent complication of drug therapy for microbial infection. It may result from opportunistic colonization following immunosuppression by the primary pathogen and can be influenced by the time interval between infections, microbial physiology, or host resistance. Experimental challenge and in vitro models are sometimes used in virulence and infectivity studies. [NIH]

Supplementation: Adding nutrients to the diet. [NIH]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Suppressive: Tending to suppress : effecting suppression; specifically : serving to suppress activity, function, symptoms. [EU]

Suppurative: Consisting of, containing, associated with, or identified by the formation of pus. [NIH]

Supraventricular: Situated or occurring above the ventricles, especially in an atrium or atrioventricular node. [EU]

Sweat: The fluid excreted by the sweat glands. It consists of water containing sodium chloride, phosphate, urea, ammonia, and other waste products. [NIH]

Sweat Glands: Sweat-producing structures that are embedded in the dermis. Each gland consists of a single tube, a coiled body, and a superficial duct. [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]

Symptomatic treatment: Therapy that eases symptoms without addressing the cause of 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]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Syphilis: A contagious venereal disease caused by the spirochete Treponema pallidum. [NIH]

Systemic: Affecting the entire body. [NIH]

Systemic disease: Disease that affects the whole body. [NIH]

Systolic: Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

Tachycardia: Excessive rapidity in the action of the heart, usually with a heart rate above 100 beats per minute. [NIH]

Tachypnea: Rapid breathing. [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]

Tau Proteins: One of the two major classes of microtubule-associated proteins isolated from the brain. The proteins have two domains: one that binds to microtubules and a second that binds to other cell components. By binding to several unpolymerized tubulin molecules simultaneously, tau proteins speed up the nucleation process in tubulin polymerization. Chemically modified tau proteins also appear to be involved in the formation and/or composition of the neurofibrillary tangles and neuropil threads found in Alzheimer disease. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

Telencephalon: Paired anteriolateral evaginations of the prosencephalon plus the lamina terminalis. The cerebral hemispheres are derived from it. Many authors consider cerebrum a synonymous term to telencephalon, though a minority include diencephalon as part of the cerebrum (Anthoney, 1994). [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]

Tenesmus: Straining, especially ineffectual and painful straining at stool or in urination. [EU]

Tetani: Causal agent of tetanus. [NIH]

Tetanic: Having the characteristics of, or relating to tetanus. [NIH]

Tetanus: A disease caused by tetanospasmin, a powerful protein toxin produced by Clostridium tetani. Tetanus usually occurs after an acute injury, such as a puncture wound or laceration. Generalized tetanus, the most common form, is characterized by tetanic muscular contractions and hyperreflexia. Localized tetanus presents itself as a mild condition with manifestations restricted to muscles near the wound. It may progress to the generalized form. [NIH]

Tetravalent: Pertaining to a group of 4 homologous or partly homologous chromosomes during the zygotene stage of prophase to the first metaphase in meiosis. [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]

Thorax: A part of the trunk between the neck and the abdomen; the chest. [NIH]

Threonine: An essential amino acid occurring naturally in the L-form, which is the active form. It is found in eggs, milk, gelatin, and other proteins. [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]

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]

Thyroid Gland: A highly vascular endocrine gland consisting of two lobes, one on either side of the trachea, joined by a narrow isthmus; it produces the thyroid hormones which are concerned in regulating the metabolic rate of the body. [NIH]

Thyrotropin: A peptide hormone secreted by the anterior pituitary. It promotes the growth of the thyroid gland and stimulates the synthesis of thyroid hormones and the release of thyroxine by the thyroid gland. [NIH]

Ticks: Blood-sucking arachnids of the order Acarina. [NIH]

Tinnitus: Sounds that are perceived in the absence of any external noise source which may take the form of buzzing, ringing, clicking, pulsations, and other noises. Objective tinnitus refers to noises generated from within the ear or adjacent structures that can be heard by other individuals. The term subjective tinnitus is used when the sound is audible only to the affected individual. Tinnitus may occur as a manifestation of cochlear diseases;

vestibulocochlear nerve diseases; intracranial hypertension; craniocerebral trauma; and other conditions. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Tissue Culture: Maintaining or growing of tissue, organ primordia, or the whole or part of an organ in vitro so as to preserve its architecture and/or function (Dorland, 28th ed). Tissue culture includes both organ culture and cell culture. [NIH]

Tissue Distribution: Accumulation of a drug or chemical substance in various organs (including those not relevant to its pharmacologic or therapeutic action). This distribution depends on the blood flow or perfusion rate of the organ, the ability of the drug to penetrate organ membranes, tissue specificity, protein binding. The distribution is usually expressed as tissue to plasma ratios. [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]

Tome: A zone produced by a number of irregular spaces contained in the outermost layer of denture of the root of a tooth. [NIH]

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]

Tooth Preparation: Procedures carried out with regard to the teeth or tooth structures preparatory to specified dental therapeutic and surgical measures. [NIH]

Topical: On the surface of the body. [NIH]

Topoisomerase inhibitors: A family of anticancer drugs. The topoisomerase enzymes are responsible for the arrangement and rearrangement of DNA in the cell and for cell growth and replication. Inhibiting these enzymes may kill cancer cells or stop their growth. [NIH]

Topotecan: An antineoplastic agent used to treat ovarian cancer. It works by inhibiting DNA topoisomerase. [NIH]

Torovirus: A genus of the family Coronaviridae characterized by enveloped, peplomer-bearing particles containing an elongated tubular nucleocapsid with helical symmetry. Toroviruses have been found in association with enteric infections in horses (Berne virus), cattle (Breda virus), and humans. Transmission takes place probably via the fecal-oral route. [NIH]

Torsion: A twisting or rotation of a bodily part or member on its axis. [NIH]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Toxicology: The science concerned with the detection, chemical composition, and pharmacologic action of toxic substances or poisons and the treatment and prevention of toxic manifestations. [NIH]

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]

Transcriptase: An enzyme which catalyses the synthesis of a complementary mRNA molecule from a DNA template in the presence of a mixture of the four ribonucleotides (ATP, UTP, GTP and CTP). [NIH]

Transcription Factors: Endogenous substances, usually proteins, which are effective in the initiation, stimulation, or termination of the genetic transcription process. [NIH]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

Transfer Factor: Factor derived from leukocyte lysates of immune donors which can transfer both local and systemic cellular immunity to nonimmune recipients. [NIH]

Transferases: Transferases are enzymes transferring a group, for example, the methyl group or a glycosyl group, from one compound (generally regarded as donor) to another compound (generally regarded as acceptor). The classification is based on the scheme "donor:acceptor group transferase". (Enzyme Nomenclature, 1992) EC 2. [NIH]

Translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Translocation: The movement of material in solution inside the body of the plant. [NIH]

Transmitter: A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [NIH]

Transplantation: Transference of a tissue or organ, alive or dead, within an individual, between individuals of the same species, or between individuals of different species. [NIH]

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]

Trichomoniasis: An infection with the protozoan parasite Trichomonas vaginalis. [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]

Trigger zone: Dolorogenic zone (= producing or causing pain). [EU]

Tropical Sprue: A condition of unknown cause. Abnormalities in the lining of the small intestine prevent the body from absorbing food normally. [NIH]

Trypsin: A serine endopeptidase that is formed from trypsinogen in the pancreas. It is converted into its active form by enteropeptidase in the small intestine. It catalyzes hydrolysis of the carboxyl group of either arginine or lysine. EC 3.4.21.4. [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]

Tube-feeding: Feeding by a tube passed into the stomach. [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]

Tubulin: A microtubule subunit protein found in large quantities in mammalian brain. It has also been isolated from sperm flagella, cilia, and other sources. Structurally, the protein is a dimer with a molecular weight of approximately 120,000 and a sedimentation coefficient of 5.8S. It binds to colchicine, vincristine, and vinblastine. [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]

Tumor suppressor gene: Genes in the body that can suppress or block the development of cancer. [NIH]

Typhimurium: Microbial assay which measures his-his+ reversion by chemicals which cause base substitutions or frameshift mutations in the genome of this organism. [NIH]

Typhoid fever: The most important member of the enteric group of fevers which also includes the paratyphoids. [NIH]

Typhoid fever: The most important member of the enteric group of fevers which also includes the paratyphoids. [NIH]

Tyramine: An indirect sympathomimetic. Tyramine does not directly activate adrenergic receptors, but it can serve as a substrate for adrenergic uptake systems and monoamine oxidase so it prolongs the actions of adrenergic transmitters. It also provokes transmitter release from adrenergic terminals. Tyramine may be a neurotransmitter in some invertebrate nervous systems. [NIH]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

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]

Urea: A compound (CO(NH2)2), formed in the liver from ammonia produced by the

deamination of amino acids. It is the principal end product of protein catabolism and constitutes about one half of the total urinary solids. [NIH]

Uremia: The illness associated with the buildup of urea in the blood because the kidneys are not working effectively. Symptoms include nausea, vomiting, loss of appetite, weakness, and mental confusion. [NIH]

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]

Urinary Retention: Inability to urinate. The etiology of this disorder includes obstructive, neurogenic, pharmacologic, and psychogenic causes. [NIH]

Urinary tract: The organs of the body that produce and discharge urine. These include the kidneys, ureters, bladder, and urethra. [NIH]

Urinary tract infection: An illness caused by harmful bacteria growing in the urinary tract. [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]

Vaccination: Administration of vaccines to stimulate the host's immune response. This includes any preparation intended for active immunological prophylaxis. [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]

Vacuole: A fluid-filled cavity within the cytoplasm of a cell. [NIH]

Vagina: The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

Vagotomy: The interruption or removal of any part of the vagus (10th cranial) nerve. Vagotomy may be performed for research or for therapeutic purposes. [NIH]

Vancomycin: Antibacterial obtained from Streptomyces orientalis. It is a glycopeptide related to ristocetin that inhibits bacterial cell wall assembly and is toxic to kidneys and the inner ear. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

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]

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]

Venereal: Pertaining or related to or transmitted by sexual contact. [EU]

Venom: That produced by the poison glands of the mouth and injected by the fangs of poisonous snakes. [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]

Ventilation: 1. In respiratory physiology, the process of exchange of air between the lungs and the ambient air. Pulmonary ventilation (usually measured in litres per minute) refers to the total exchange, whereas alveolar ventilation refers to the effective ventilation of the alveoli, in which gas exchange with the blood takes place. 2. In psychiatry, verbalization of one's emotional problems. [EU]

Ventilator: A breathing machine that is used to treat respiratory failure by promoting ventilation; also called a respirator. [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]

Vertebrae: A bony unit of the segmented spinal column. [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]

Vesicular Exanthema of Swine: A calicivirus infection of swine characterized by hydropic degeneration of the oral and cutaneous epithelia. [NIH]

Vesicular Exanthema of Swine Virus: The type species of the genus Calicivirus, an RNA virus infecting pigs. The resulting infection is an acute febrile disease which is clinically indistinguishable from foot and mouth disease. Transmission is by contaminated food. [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]

Villous: Of a surface, covered with villi. [NIH]

Villus: Cell found in the lining of the small intestine. [NIH]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Viral vector: A type of virus used in cancer therapy. The virus is changed in the laboratory and cannot cause disease. Viral vectors produce tumor antigens (proteins found on a tumor cell) and can stimulate an antitumor immune response in the body. Viral vectors may also be used to carry genes that can change cancer cells back to normal cells. [NIH]

Virion: The infective system of a virus, composed of the viral genome, a protein core, and a protein coat called a capsid, which may be naked or enclosed in a lipoprotein envelope called the peplos. [NIH]

Virulence: The degree of pathogenicity within a group or species of microorganisms or viruses as indicated by case fatality rates and/or the ability of the organism to invade the tissues of the host. [NIH]

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]

Virus Replication: The process of intracellular viral multiplication, consisting of the synthesis of proteins, nucleic acids, and sometimes lipids, and their assembly into a new infectious particle. [NIH]

Visceral: , from viscus a viscus) pertaining to a viscus. [EU]

Visceral Afferents: The sensory fibers innervating the viscera. [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]

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]

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]

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]

Windpipe: A rigid tube, 10 cm long, extending from the cricoid cartilage to the upper border of the fifth thoracic vertebra. [NIH]

Withdrawal: 1. A pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality

disorders. 2. (DSM III-R) A substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

Wound Healing: Restoration of integrity to traumatized tissue. [NIH]

Wound Infection: Invasion of the site of trauma by pathogenic microorganisms. [NIH]

Xanthomatosis: A condition of morphologic change in which there is accumulation of lipids in the large foam cells of tissues. It is the cutaneous manifestation of lipidosis in which plasma fatty acids and lipoproteins are quantitatively changed. The xanthomatous eruptions have several different distinct morphologies dependent upon the specific form taken by the disease. [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]

Yellow Fever: An acute infectious disease primarily of the tropics, caused by a virus and transmitted to man by mosquitoes of the genera Aedes and Haemagogus. [NIH]

Yellow Fever Virus: The type species of the Flavivirus genus. Principal vector transmission to humans is by Aedes spp. mosquitoes. [NIH]

Zygote: The fertilized ovum. [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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