# Antibiotics

A 3-in-1 Medical Reference

Medical Dictionary

Bibliography &

Annotated Research Guide

to Internet References

ICON Group International, Inc.

# ANTIBIOTICS

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

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# FORWARD

In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[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 antibiotics 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 antibiotics, 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 antibiotics, 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 antibiotics. 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 antibiotics, 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 antibiotics.

*The Editors*

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

# CHAPTER 1. STUDIES ON ANTIBIOTICS

## Overview

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

## The Combined Health Information Database

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

- **Acute Otitis Media: Part II. Treatment in an Era of Increasing Antibiotic Resistance**

  Source: American Family Physician. 61(8): 2410-2416. April 15, 2000.

  Contact: Available from American Academy of Family Physicians. 11400 Tomahawk Creek Parkway, Leawood, KS 66211-2672. (800) 274-2237. Website: www.aafp.org.

  Summary: Antibiotic resistance is increasing among the pathogens that commonly cause acute otitis media (AOM, middle ear infection). This article is the second in a series on AOM. The author notes that this increase in antibiotic resistance may require changes in the traditional antibiotic treatment of AOM. Risk factors for resistant pathogens include recent antibiotic treatment of AOM, children in day care facilities, wintertime infections, and AOM in children less than 2 years of age. Amoxicillin remains the antibiotic of first choice, although a higher dosage (80 mg per kg per day) may be indicated to ensure

eradication of resistant Streptococcus pneumonia. Oral cefuroxime or amoxicillin clavulanate and intramuscular ceftriaxone are suggested second line choices for treatment failure. Compliance with antibiotic regimens is enhanced by selecting agents that require less frequent dosing (such as one or two times a day) and by prescribing shorter (five days or less) treatment courses. Selective use of tympanocentesis if the patient does not respond to empiric therapy can help confirm the diagnosis and guide effective therapy. 2 figures. 2 tables. 30 references.

- **Five vs. Ten Days of Antibiotic Therapy for Acute Otitis Media in Young Children**

  Source: Pediatric Infectious Disease Journal. 19(5): 458-463. May 2000.

  Contact: Available from Lippincott Williams and Wilkins. 12107 Insurance Way, Hagerstown, MD 21740. (800) 637-3030. Fax (301) 824-7390. Website: www.lww.com.

  Summary: Many publications in recent years have argued in favor of shortened therapy for acute otitis media (AOM, middle ear infection). However, doubt persists regarding children younger than 2 years, and some authors therefore resist short course therapy to children older than 2 years. This article reports on a study that compared five versus ten days of antibiotic therapy for AOM in young children (cefpodozime proxetil, 8 mg per kg per day). Between October 1996 and April 1997, 450 children (mean age, 14.3 months) were enrolled in the study; 227 children in the 5 day group (followed by a 5 day placebo period) and 223 in the 10 day group. Clinical success was obtained on Days 12 to 14 after the beginning of treatment in 175 (84.1 percent) of the 208 children receiving the 5 day regimen, and in 194 (92.4 percent) of the 210 children receiving the 10 day regimen. The superiority of the standard regimen (10 days) was more marked among children cared for outside their homes (92.5 percent versus 81.5 percent). Clinical success persisted on Days 28 to 42 among 134 (85.4 percent of the 157 assessable patients in the 5 day group, and in 144 (83.7 percent) of the 172 assessable patients in the 10 day group. The authors conclude that the 10 day regimen resulted in a higher success rate at the conclusion of therapy, but there were no differences between the two study groups 4 to 6 weeks after enrollment in the study protocol. 5 tables. 23 references.

- **What Role for Antibiotics in Otitis Media and Sinusitis?**

  Source: Postgraduate Medicine. 104(3): 93-99, 103-104. September 1998.

  Contact: Available from Postgraduate Medicine. P.O. Box 459, Hightstown, NJ 08520-9201. (609) 426-7070. Fax (609) 426-7087.

  Summary: Patients often expect to be given antibiotics for any illness affecting the ears and sinuses, regardless of whether such treatment is warranted. This article, the fourth of four articles on common ear, nose, and throat (ENT) problems, discusses the role for antibiotics in treating otitis media (middle ear infection) and sinusitis (sinus infection). The authors caution that bacterial resistance to antibiotics is rising. They outline the types of otitis media and sinusitis that should be treatment with antibiotics and the agents that are currently the most effective for each condition. The authors review the established classification and treatment guidelines for these conditions. First-line treatment for both uncomplicated acute otitis media and acute sinusitis is amoxicillin. Erythromycin ethylsuccinate and sulfisoxazole or TMP-SMZ may be used in patients who are allergic to penicillin. Beta-lactamase-stable agents should be given when no response occurs within 48 to 72 hours. In cases where penicillin-resistant pneumococcus is suspected, high-dose amoxicillin, with or without clavulanate, or clindamycin should be considered. Antibiotics are not indicated for initial treatment of otitis media with effusion (OME), but may be considered for effusions lasting longer than 3 months.

Prophylactic antibiotics should be considered only for recurrent acute infections occurring three or more times within 6 months or four or more times with a year. 4 tables. 27 references. (AA-M).

- **Randomized Controlled Trial of Point-of-Care Evidence to Improve the Antibiotic Prescribing Practices for Otitis Media in Children**

  Source: Pediatrics. 107(2): [e15]. February 2001.

  Contact: Available from American Academy of Pediatrics. 141 Northwest Point Boulevard, Elk Grove Village, IL 60007-1098. (888) 227-1773. Fax (847) 434-8000. E-mail: journals@aap.org. Website: www.pediatrics.org. Full text of this article is available at www.pediatrics.org/cgi/content/full/107/2/e15.

  Summary: Prescribing practices for otitis media (middle ear infection) are not consistent with current evidence based recommendations. So contend the authors of this research study that was undertaken to determine whether point of care evidence delivery regarding the use and duration of antibiotics for otitis media decreases the duration of therapy from 10 days and decreases the frequency of prescriptions written. The study used a point of care message system (a computer prescription writer software program) as the intervention. Intervention providers had a 34 percent greater reduction in the proportion of time they prescribed antibiotics for less than 10 days. Intervention providers were less likely to prescribe antibiotics than were control providers. The authors conclude that the point of care information system integrated into pediatric outpatient care can significantly influence provider behavior for a common condition. 1 figure. 2 tables. 21 references.

- **Routine Antibiotics: Are They Really Needed for Acute Otitis Media?**

  Source: JAAPA. Journal of the American Academy of Physician Assistants. 11(10): 41-42, 45. October 1998.

  Contact: Available from Medical Economics. 5 Paragon Drive, Montvale, NJ 07645-1742. (800) 432-4570.

  Summary: This article considers the use of routine antibiotics in the treatment of acute otitis media (ear infection). The author states that otitis media is overdiagnosed and overtreated, and explains his reasons for this conclusion. The author discusses antibiotic use in the U.S. compared to that in Europe, the fear of complications of otitis media (such as meningitis, mastoiditis, and hearing loss), the role of worry over malpractice action, otitis media that is virus induced (for which antibiotics will not be effective), growing worldwide bacterial resistance to antibiotics, the effective management of parents whose children have ear infections, and the shifting to more conservative management of acute otitis media by restricting initial use of antimicrobials. One sidebar offers ten recommendations for the better management of acute otitis media (AOM), including the use of antibiotics but in a more conservative fashion. 10 references.

- **Treatment of Acute Otitis Media with a Shortened Course of Antibiotics: A Meta-Analysis**

  Source: JAMA. Journal of the American Medical Association. 279(21): 1736-1742. June 3, 1998.

  Summary: This article reports on a meta analysis of randomized controlled trials of antibiotic treatment of acute otitis media (AOM) in children; the analysis was

undertaken to determine whether outcomes were comparable in children treated with antibiotics for less than 7 days or at least 7 days or more. The authors conducted MEDLINE, EMBASE, Current Contents, and Science Citation Index searches to identify randomized controlled trials of the treatment of AOM in children with antibiotics of different durations. Trial methodological quality was assessed independently by 7 reviewers; outcomes were extracted as the number of treatment failures, relapses, or reinfections. The summary odds ratio for treatment outcomes (measured at 8 to 19 days posttreatment) in children treated with short acting antibiotics for 5 days versus those treated for 8 to 10 days was 1.52; however, by 20 to 30 days posttreatment, the outcomes between treatment groups were comparable. The authors conclude that 5 days of short acting antibiotic use is effective treatment for uncomplicated AOM in children. 2 figures. 2 tables. 88 references.

- **Therapy for Acute Otitis Media: Preference for Oral or Parenteral Antibiotic**

  Source: Otolaryngology Journal Club Journal. 3(5): 282-285. October 1996.

  Summary: This article reports on a study undertaken to determine if parents prefer single-dose intramuscular therapy or standard 10-day oral therapy for the treatment of acute otitis media. In a randomized, controlled trial from October 1993 to May 1994 in private practice patients at 15 sites in the U.S., 648 children aged 3 months to 6 years with acute otitis media (AOM) were randomly assigned to receive a single dose of intramuscular (IM) ceftriaxone sodium or 10 days of oral amoxicillin and clavulanate potassium. Parents were asked which treatment they would prefer for their child at the time of enrollment in the study and were contacted to answer questions about treatment 3-5 days after the beginning of treatment and at 14-16 days when the physician examined the child for resolution of symptoms. The authors report on parent satisfaction, parental loss of sleep, work or sleep absences, and future preference for method of administration. The authors conclude that parents prefer single-dose IM therapy over standard 10-day oral therapy for AOM. Indications for single-dose ceftriaxone for AOM include emesis, concurrent bacteremia, concern about compliance, and pending family travel. 3 tables. 2 references. (AA-M).

- **Acute Otitis Media: Update on How and When to Give Antibiotics**

  Source: Consultant. 36(4): 721-728. April 1996.

  Summary: This article updates readers on the use of antibiotic therapy for acute otitis media (AOM) in children. The authors note that the emergence and global spread of antibiotic-resistant bacteria have prompted a thoughtful re-evaluation of optimal diagnostic criteria and indications for treatment. Diagnosis is most certain when the tympanic membrane is discolored, bulging, and immobile. Once the diagnosis of AOM is established, antibiotic treatment is a reasonable, but not necessary, option. Amoxicillin remains the drug of first choice; trimethoprim-sulfamethoxazole is an appropriate second choice for apparent treatment failure due to beta-lactamase-producing bacteria. The authors stress that the goal in AOM is effective treatment while decreasing the impact of antbiotic therapy on the selection of resistant pathogens. This can be achieved through accurate diagnosis of AOM, coupled with judicious use of antibiotics and a decreased duration of therapy. 2 figures. 2 tables. 31 references. (AA-M).

- **Use of Antibiotics in Preventing Recurrent Acute Otitis Media and in Treating Otitis Media with Effusion: A Meta-Analytic Attempt to Resolve the Brouhaha**

  Source: Journal of the American Medical Association. 270(11): 1344-1351. 1993.

Summary: This article, written for health professionals, is a review of selected studies that were looked at to determine the efficacy of antibiotics for prophylaxis of recurrent otitis media and treatment of otitis media with effusion in children. Results of this review indicated that antibiotics appear to have beneficial but limited effect on recurrent otitis media and short-term resolution of otitis media with effusion. Longer-term benefit for otitis media with effusion has not been shown. Bibliographic references are included.

- **Antibiotic Misuse Resulting in Drug Resistance**

  Source: Advance for Speech-Language Pathologists and Audiologists. 5(1): 6. January 9, 1995.

  Contact: Available from Merion Publications, Inc. 650 Park Avenue West, King of Prussia, PA 19406. (800) 355-1088.

  Summary: This brief article addresses the problem of antibiotic misuse resulting in drug resistance. The author interviews several prominent researcher-physicians, gathering and providing information about the areas in which antibiotics are being misused; the natural process of resistance; how beta-lactam antibiotics kill an infectious bacteria; problems with bacteria that are completely unaffected by available antibiotics, including the Enterococcus species, or hospital bacterium; infection control issues; bacteria that are responsible for otitis media; a new antibiotic used to treat otitis media, Biaxin; the use of antibiotics in plants or animals to increase size or to kill infection; and steps that patients and physicians can take to avoid the increase and spread of resistant bacteria. The telephone numbers and addresses of the three physicians interviewed are included.

- **Antibiotics for Rheumatoid Arthritis?: Minocycline Shows Promise in Some Patients**

  Source: Postgraduate Medicine. 105(4): 95-98. April 1999.

  Summary: This journal article provides health professionals with information on the use of the antibiotic minocycline for the treatment of rheumatoid arthritis. Although studies in the United States and Europe have validated the usefulness of minocycline, most rheumatologists are not convinced of the value of antibiotic therapy for this form of arthritis. Three double-blind, controlled studies and two open trials have reported the efficacy of minocycline in treating rheumatoid arthritis. The mechanism of action of minocycline and related compounds is unclear; however, the antirheumatic effect could be related to immunomodulatory and anti-inflammatory properties. Minocycline may be a reasonable alternative for treating patients with a benign prognosis, but not for those with severe and potentially very destructive disease. 3 tables and 25 references.

## Federally Funded Research on Antibiotics

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

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[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).

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 antibiotics.

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

- **Project Title: A GENETIC SCREEN FOR PROTEIN EVOLUTION AND PROTEOMICS**

  Principal Investigator & Institution: Cornish, Virginia W.; Chemistry; Columbia Univ New York Morningside 1210 Amsterdam Ave, Mc 2205 New York, Ny 10027

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

  Summary: (provided by applicant): This grant application describes a cell-based assay for detecting molecular recognition and catalysis that can be used to evolve proteins with new functions. There is tremendous interest in being able to engineer proteins with new specificities and new activities for use as reagents for biomedical research, diagnostics and therapeutics for the health care community, and tools for the pharmaceutical industry. The screen builds from existing technology for dimerizing proteins inside a cell with dimeric ligands via the ligands' receptors (CIDs). By replacing one of the ligand-receptor pairs with potential binding partners, binding can be detected. By replacing the chemical linker between the two ligands with a bond and adding an enzyme, the assay can be used as a read-out for bond formation or bond cleavage. In Preliminary Results dexamethasone-methotrexate CIDs with non-cleavable and cleavable linkers have been developed. Aim 1 outlines our plans to evolve a protein receptor for estradiol that can be used in medical diagnostics for monitoring estrogen levels in women. We have developed a docking algorithm to pick several monomeric proteins from the PDB as the starting protein scaffolds. We plan to mutagenize these proteins using existing methods and then select for high affinity, specific receptors by screening for binding to estradiol and against binding to other common steroids. Aim 2 describes our plans to modify the yeast two-hybrid assay to detect catalysis and then evolve a penicillin-binding protein into a cephalosporinase enzyme. Penicillin-binding proteins are the target of penicillin **antibiotics** and are believed to be the evolutionary precursors of cephalosporinases, the bacterial resistance enzymes that hydrolyze and inactivate these **antibiotics.** Because of the evolutionary relationship, the PBPs present a tractable first target for enzyme evolution. Moreover, this project should provide insight into how bacteria evolve **antibiotic** resistance and the mechanism by which the resistance enzymes hydrolyze the **antibiotic.** Finally, in Aim 3, we propose to develop a bacterial CID so that future protein evolution experiments can be carried out in bacteria. Bacteria have faster doubling times and higher transformation efficiencies than yeast, and so a bacterial CID system should facilitate the evolution experiments.

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

- **Project Title: A PRACTICAL SYNTHETIC ROUTE TO THE TETRACYCLINES**

  Principal Investigator & Institution: Myers, Andrew G.; Professor; Chemistry and Chemical Biology; Harvard University Holyoke Center 727 Cambridge, Ma 02138

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

Summary: (Principal Investigator's Abstract) The objective of this proposal is to develop the first practical, efficient, and enantioselective laboratory synthetic route(s) to the tetracycline **antibiotics.** The goal is to devise a route of twelve or fewer synthetic steps, perhaps as few as eight steps, beginning with benzoic acid as a starting material. A constraint that the synthetic route be versatile is also imposed, allowing for the introduction of substantive structural variability at a late stage, particularly within the C and D rings of the tetracycline structure, where prior research has shown that there is great opportunity for **antibiotic** development. Synthesis of a wide range of new tetracyclines for evaluation as improved **antibiotics** and, potentially antitumor agents is proposed. A particular focus is the development of effective **antibiotics** against tetracycline-resistant microorganisms. Adaptation and/or modification of these synthetic routes to target new tetracycline structures with antitumor activity, such as SF-2575 (TAN-1518 X) will also be attempted.

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

- **Project Title: ALPHA HELICAL CATHELICIDINS AND HOST DEFENSE**

  Principal Investigator & Institution: Lehrer, Robert I.; Professor; Medicine; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2001; Project Start 01-JUN-1999; Project End 31-MAY-2004

  Summary: Description (adapted from applicant's abstract): Long term objectives. To define antimicrobial molecules involved in innate immunity, learn how they work, and use this knowledge to create novel ways to prevent and treat infections.	Specific aims. 1). To purify human hCAP-18 from leukocytes and secretions and examine its properties. 2) To learn how hCAP-18 and its murine homologue are processed by leukocytes. 3) To study the structures of human LL-37, murine CRAMP-38, and high molecular weight forms of hCAP-18 from plasma and secretions. 4) To define the minimal peptide structure required for LPS-binding and antimicrobial activity against P. aeruginosa. 5) To examine the effects of LPS and other stimuli on in vitro expression of hCAP-18 and examine in vivo synthesis of CRAMP in LPS-treated mice. 6) To measure hCAP-18 levels in secretions, and examine its interactions with other host defense peptides. Methods. These will include peptide synthesis, protein purification by preparative electrophoresis and chromatography (gel permeation, ion exchange, RP-HPLC and affinity), computer modeling, CD and FTIR measurements, antimicrobial testing and Northern and RT-PCR analyses. Health relatedness. The innate immune system is a key element of mucosal immunity that plays a major role in preventing infection. The proposal centers on two newly discovered, pro-antibiotics ("cathelicidins"): human hCAP-18 and its murine homologue, CRAMP. These peptides are expressed constitutively by leukocytes, are produced by epithelial cells, and are found in secretions such as human milk, tears and semen. Their C-terminal domains bind LPS avidly and have potent activity against P. aeruginosa and other pathogens, even under high salt condition. The experiments will expand our knowledge about these important peptides, and should provide the information needed to develop them as **antibiotics** for topical bronchopulmonary use in cystic fibrosis.

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

- **Project Title: ANTIBIOTIC HYPERSUSCEPTIBILITY MUTATIONS IN BACTERIA**

  Principal Investigator & Institution: Neyfakh, Alex A.; Associate Professor; Medicinal Chem & Pharmacognosy; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

Timing: Fiscal Year 2002; Project Start 15-FEB-2002; Project End 31-JAN-2006

Summary: (Adapted from the Applicant's Abstract): The escalating problem of bacterial resistance to **antibiotics** calls for radical changes in the existing antibacterial therapies. One of the most promising approaches is the use of **antibiotic** potentiators, compounds that make bacterial cells hypersusceptible to **antibiotics.** The goal of the project is to identify multiple novel molecular targets for potentiators. This will be accomplished by isolating **antibiotic** hypersusceptibility mutations of Gram-negative bacteria, Acinetobacter and/or Escherichia coli. These mutations will specify bacterial proteins whose inhibition is likely to potentiate antimicrobial action of **antibiotics. Antibiotic** hypersusceptibility is a very difficult phenotype to select, and only few such mutations are known. We have designed and tested a novel genetic strategy for selection of hypersusceptibility mutations, termed SDR. Application of this strategy will identify multiple mutations increasing bacterial susceptibility to beta-lactams (ampicillin, ceftazidime, imipenem), translational inhibitors (erythromycin, linezolid, tetracycline, and chloramphenicol) and fluoroquinolone **antibiotics** (ciprofloxacin). The molecular mechanisms underlying the effects of the most interesting of these mutations will be analyzed. In addition to identifying promising targets for potentiators, the project will help unravel new aspects of the mechanism of action of **antibiotics** and new features of bacterial physiology.

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

- **Project Title: ANTIBIOTIC SUSCEPTIBILITY OF BACTERIA IN BIOFILMS**

  Principal Investigator & Institution: Stewart, Philip S.; Deputy Director & Research Coordinator; Chemical Engineering; Montana State University (Bozeman) Bozeman, Mt 59717

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

  Summary: (provided by applicant): When bacteria attach to a surface and grow as a biofilm they are protected from killing by **antibiotics.** Biofilm formation is increasingly recognized as a factor in the persistence of varied infections. The goal of this project is to complement ongoing experimental investigations of **antibiotic** resistance in biofilms by developing the first comprehensive, phenomenological model of biofilm reduced susceptibility to killing by **antibiotics.** An existing mathematical model of biofilm development will be expanded to include four hypothesized protective mechanisms. These mechanisms address retarded **antibiotic** penetration, reduced metabolic activity or growth in parts of the biofilm due to local nutrient depletion, stress response activation by some biofilm bacteria, and differentiation of some biofilm cells into a dormant persister state analogous to spore formation. The model will be improved by developing mathematical expressions for the release of cells from the biofilm based on a mechanical analysis of the biofilm as a viscoelastic fluid. Finally, model results will be compared to experimental data. Experiments will be performed to measure spatio-temporal responses, including both killing and detachment, to **antibiotic** treatment in a P. aeruginosa experimental system, and these results will be compared with output of the mathematical model. Progress in understanding the stubborn persistence of biofilm infections in the face of **antibiotic** chemotherapy has been surprisingly slow. This modeling effort will accelerate this effort by integrating the many constituent phenomena that must be considered and serving as a vehicle for dialogue between the diverse disciplines that must communicate to solve this problem. The model will ultimately be a tool for investigating the consequences of hypothesized resistance mechanisms, designing experiments to test these mechanisms, identifying novel treatment strategies, and determining optimal **antibiotic** dosing protocols. This project

will afford a rich interdisciplinary training experience for the three participating graduate students.

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

- **Project Title: ANTIBIOTICS IN INFANCY-RISK FACTOR FOR CHILDHOOD ASTHMA**

  Principal Investigator & Institution: Ownby, Dennis R.; Head; Pediatrics; Medical College of Georgia 1120 15Th St Augusta, Ga 30912

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

  Summary: (Provided by Applicant) Morbidity and mortality from childhood asthma have been increasing in all developed countries over the past three decades, including in the United States. Numerous theories have been advanced to explain this asthma epidemic, but no single theory has held up to careful scrutiny. Recent international studies have suggested a relatively strong causal relationship between increased risk of childhood asthma and exposure to **antibiotics** during childhood, especially during the first year of life. The increased asthma risk was seen whether **antibiotics** were used to treat respiratory or non-respiratory infections. While these previous studies are suggestive, there are significant methodologic concerns about each study. A major concern with most of the studies is their reliance on retrospective recall of **antibiotic** exposure data from parents years after the exposure. We have data from a prospective, NIH-funded study of the relationship between early environmental exposures and the development of asthma in a birth cohort of children followed to an average 6.7 years of age. At 6.7 years, 482 (58%) of the original 833 children were clinically examined as part of this Childhood Asthma Study (CAS). In addition to clinical histories, the 6- to 7- year clinical examination included skin tests, IgE antibody tests, pulmonary function tests and methacholine challenge. At entry all of the CAS children were within the Health Alliance Plan (HAP) HMO. The current proposal is based on combining the CAS data set with pharmacy data extracted from the HAP data archives. This will allow us to examine possible relationships between **antibiotic** use, as determined by prescriptions filled, and asthma at 6 to 7 years of age. While not strictly a prospective study, these methods will avoid many of the potential sources of bias found in previous studies. We will also be able to evaluate any relationships between **antibiotic** exposure and asthma for confounding by other risk factors such as bedroom allergen levels, pet ownership, cigarette smoke exposure, and parental history of asthma or allergy. The proposed study is entirely separate from the goals of the original grant which did not consider **antibiotic** use as a potential risk factor for asthma or allergy. This new analysis will allow a much more rigorous examination of the possible relationship between early **antibiotic** use and asthma in a population of American children.

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

- **Project Title: ANTITUMOR ANTIBIOTICS**

  Principal Investigator & Institution: Boger, Dale L.; Professor; Scripps Research Institute 10550 N Torrey Pines Rd La Jolla, Ca 920371000

  Timing: Fiscal Year 2001; Project Start 01-FEB-1986; Project End 31-JAN-2004

  Summary: Abstract: Studies on the total synthesis and evaluation of anti-tumor **antibiotics** including bleomycin A/2, phomazarin, roseophilin, ningalin A. lamellarin O, lukianol A, storniamide A, anhydrolycorinone, hippadine, anhydrolycorinium chloride, rebeccamycin, (20S)-camptothecin, vindoline (vincristine/vinblastine), rubrolone, and key structural analogs are detailed. In the course of these studies, the

investigation, development, and implementation of: (1) heteroaromatic azadiene Diels-Alder reactions, (2) the LUMO/diene-controlled Diels-Alder reactions of N-sulfonyl-l-aza- 1,3-butadienes, (3) the intramolecular Diels-Alder reactions of O-methyl alpha, beta-unsaturated oximes, (4) the thermal reactions of cyclopropenone ketals including those of reversibly generated pi- delocalized singlet vinylcarbenes, (5) tandem Diels-Alder/1,3-dipolar cycloadditions of 1,3,4-oxadiazoles, and (6) acyl radical alkene addition reactions will be pursued and provide the opportunity to comprehensively extend past studies. An additional application of the synthetic methodology to the preparation of pyridoxol is described. The proposed studies include the examination of anti-tumor **antibiotics** that mediate their cellular effects through sequence selective DNA binding and provide well-defined problems on the design, preparation, and evaluation of synthetic, mechanism-based anti-tumor agents in which fundamental studies of their structural features responsible for DNA binding affinity, selectivity, and functional reactivity may be addressed.

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- **Project Title: ASSEMBLY OF THE DIVISION SEPTUM IN ESCHERICHIA COLI**

  Principal Investigator & Institution: Weiss, David S.; Professor; Microbiology; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2001; Project Start 01-AUG-1999; Project End 31-JUL-2004

  Summary: The long-term focus of our work is cell division in bacteria. In particular, we are interested in how the division septum is formed, and how its formation is coordinated with other events in the cell- cycle such as chromosome segregation. An ancillary objective is to understand how proteins are localized to specific subcellular sites. This interest stems from the observation that many proteins involved in septum assembly are localized to the division site. Cell division and protein localization are fundamental cellular processes of importance to all organisms, including humans, and underlie diseases such as cancer, but are often difficult to study due to technical limitations. The wealth of genetic tools available in Escherichia coli makes this an ideal model organism for studies of basic cellular processes. Septum assembly in E. coli requires at least nine essential proteins, all of which localize to the division site. Our hypothesis is that these proteins form of complex that contains all of the activities need for septum assembly, and that interactions among these proteins are important for their recruitment to the division site and for regulating their activities. Thus, we want to know more about the detailed function of these proteins, to identify interactions among these proteins, and to know whether the set is complete. To approach these issues we will characterize FtsI, a membrane protein with an enzymatic activity (transpeptidase) related to peptidoglycan synthesis. Specifically, we will (i) use a combination of genetics and fluorescence microscopy to identify sequences in FtsI that target this protein to the division site; (ii) use biochemical and genetic approaches to look for proteins that interact directly with FtsI; and (iii) use fluorescence microscopy to determine the subcellular location of three transglycosylases postulated to be involved in synthesis of septal peptidoglycan and to interact with FtsI. A better understanding of cell division in a simple bacterial system might shed light on these processes in other organisms, including humans. In addition, a better understanding of these processes might lead to more knowledge-based approaches to developing new **antibiotics.** In this regard, it is worth noting that four of the proteins to be studied here (FtsI and the three transglycosylases) are primary targets of beta-lactam **antibiotics.**

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

- **Project Title: ASYMMETRIC SYNTHESIS OF MACROLIDE ANTIBIOTICS**

  Principal Investigator & Institution: Leighton, James L.; Associate Professor; Chemistry; Columbia Univ New York Morningside 1210 Amsterdam Ave, Mc 2205 New York, Ny 10027

  Timing: Fiscal Year 2001; Project Start 01-AUG-1998; Project End 31-JUL-2002

  Summary: (Principal Investigator's) This proposal details the development of new, catalytic reaction methodology for the efficient asymmetric synthesis of polyacetate-derived macrolide **antibiotics** of potential pharmaceutical interest such as recently discovered powerfully anti-fungal marine natural product leucascandrolide A. It has been documented that drug-resistant bacterial and fungal infections represent a problem of rapidly growing importance. More than simply achieving synthesis of such compounds, the focus of the proposal is on advancing the frontiers of efficiency, waste-minimizing and economic viability of such synthetic efforts. The ultimate goal is thus the realization of practicable and practical chemistry that will affect both the discovery and process phases of research into new medicinal agents. These reactions under consideration have as their unifying theme the stereo-and regioselective transition metal-catalyzed carbonylation of alkenes leading to the direct synthesis of suitably protected/masked 3,5- dihydroxyaldehydes. This represents a novel approach to (1,3,5.) polyol synthesis that will enjoy the benefits that render carbonylation a feasible industrial-scale process.

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

- **Project Title: ASYMMETRIC SYNTHESIS OF VANCOMYCIN ANTIBIOTICS**

  Principal Investigator & Institution: Evans, David A.; Professor; Chemistry and Chemical Biology; Harvard University Holyoke Center 727 Cambridge, Ma 02138

  Timing: Fiscal Year 2001; Project Start 01-APR-1990; Project End 31-MAR-2003

  Summary: The first member of the vancomycin family of peptide **antibiotics** was isolated in 1956, and the progenitor of the family, vancomycin, has been in clinical use for more than twenty-five years as an **antibiotic** of last resort. The continuing objective of this research program is to develop efficient approaches to the synthesis of the principal members of the vancomycin family of **antibiotics.** Accordingly, we will pursue laboratory syntheses of vancomycin and the related congeners eremomycin, ristocetin, teicoplanin, and aridicin A. In conjunction with the execution of these objectives, we will develop new methods for the asymmetric synthesis of complex amino acids and cyclin peptides. In addition, we propose to develop new methodology for the oxidative macrocyclization of phenol-containing peptides to form macrocyclic diphenyl ethers and biphenyls, critical constituents of the vancomycin skeleton. The successful development of this methodology will enable us to pursue a biogenetically modeled synthesis of virtually any member of the vancomycin family. During the course of this project we intend to confirm (correct) the absolute stereochemical assignments of the principal members of this family by total synthesis.

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

- **Project Title: BACTERIAL DNA POLYMERASES: TARGETS FOR NOVEL ANTIBIOTIC**

  Principal Investigator & Institution: Butler, Michelle M.; Microbiotix, Inc. 1 Innovation Dr Worcester, Ma 01605

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

Summary: (Applicant's abstract): The objective of this project is to identify novel drugs to treat antibiotic-resistant Gr+ and Gr- bacterial infections. The work will utilize an unexploited target, the class III bacterial DNA polymerase (pol III). The bacterial pol IIIs are highly conserved enzymes that are required for the synthesis of DNA during chromosomal replication. When an inhibitor of pol III is applied to a growing bacterium, it stops replication, and, thus, like the replication-specific quinolone **antibiotics,** it is bactericidal. Furthermore, the pol III-selective inhibitors are equally effective against clinically relevant antibiotic-resistant and antibiotic-sensitive pathogens. Therefore, they provide an excellent basis for developing novel agents, which are effective in the treatment of antibiotic-resistant infections. The research plan for the phase I studies proposes to identify novel inhibitors via moderate throughput screening of diverse chemical libraries against three pol IIIs (the Gr- pol III E, and the Gr+ E and C types). The goal of this screening will be to identify one or more novel chemical scaffolds that can be suitably modified for development as new bactericidal drug candidates. Health relatedness: The project exploits a novel target to identify new bactericidal compounds to confront the growing crisis in the therapy of infections caused by antibiotic-resistant bacterial pathogens. PROPOSED COMMERCIAL APPLICATION: Microbiotix will identify bactericidal inhibitors of Gr+ and Gr- pathogens with strong potential for development as broad-spectrum antimicrobials effective in the treatment of problematic antibioticresistant infections. The SBIR phase I study proposes to identify distinct pharmacophores selective for one or more of the three Gr+ and Gr- specific pol Ms. In phase II Microbiotix will chemically modify and further develop these pol III-specific pharmacophores into bona fide drug candidates

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- **Project Title: BACTERICIDAL AGENTS FOR SLOW-GROWING BACTERIA**

  Principal Investigator & Institution: Markham, Penelope N.; Director of Research; Influx, Inc. 2201 W Campbell Park Dr Chicago, Il 60612

  Timing: Fiscal Year 2003; Project Start 01-MAY-2003; Project End 31-OCT-2004

  Summary: (provided by applicant): In many chronic infections, including all biofilm related infections, the slow growth of bacteria is believed to account not only for resistance to **antibiotics,** but also for the high incidence of persistence and relapse. Considering that all currently prescribed **antibiotics** are significantly more effective against rapidly growing pathogens, the development of **antibiotics** highly effective against bacteria in the slow mode of growth is of utmost importance. By screening a chemical library for compounds bactericidal for slow-growing S. aureus, we have succeeded in identifying a very promising class of compounds, pyridinium thiol ethers (PTEs). Preliminary data indicate that PTEs are not only effective against fluid-phase S. aureus, but also against biofilms as well as against other bacteria in a slow mode of growth. In the proposed Phase I project, we will synthesize and screen a library of PTEs in order to identify compounds that will be bactericidal against slow and logarithmically growing S. aureus. Feasibility of the medical use of the most active derivatives will be analyzed. Finally, the basic principles underlying the molecular mechanism of action of PTE compounds will be investigated. The Phase I project will provide the basis for the Phase II project, which will involve chemical improvement of the lead compounds, investigation of their activity in various biofilm models, and in vivo toxicology studies. PTE compounds could provide a unique opportunity for eradication of infections associated with slow bacterial growth.

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- **Project Title: BETA-DEFENSINS IN CARIES PRONE CHILDREN**

  Principal Investigator & Institution: Dale-Crunk, Beverly A.; Professor; University of Washington Seattle, Wa 98195

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

  Summary: The beta-defensins are natural **antibiotics** by oral epithelia and secreted in saliva. These peptides have broad specificity against bacteria, fungi, and some viruses. They are thought to have role in oral health as natural **antibiotics.** Beta-defensin levels may between individuals, and those with defects in the expression or function of beta-defensins may be susceptible to recurrent infection. Dental caries is an infection; individuals and populations have differing susceptibility to caries. Caries risk is thought to be due to bacterial exposure, diet, and cultural behaviors, but may also be related to biological factors that are due to genetic differences. Beta-defensins may have multiple potential effects on bacteria that colonize the tooth surface, altering biofilm formation, acting directly on bacterial survival, and acting synergistically with other anti-microbial factors. Previous observations on activity, localization and secretion of beta-defensins lead to the hypothesis that the beta-defensins, hBD-1, may be associated with risk for dental caries and that low expression levels, or genetic changes in the function or expression of the peptide, could place an individual at risk for caries. This laboratory has established immunoassays for hBD-1 expression in gingiva and saliva, determined multiple single nucleotide polymorphisms (SNPs) in the DEFB1 gene encoding hBD-1, and examined SNP frequency in different ethnic groups. For this study we have identified a population of Hispanic children in Toppenish, WA, a rural agricultural community near Heritage College, a minority institution that serves Hispanic and Native American students. Appropriately 35% of these children have had 4 or more caries, while nearly 40% gave had no caries. Using these preliminary findings and new SNP assays, the goal of this proposal is to conduct a case- control study to explore the relationship between hBD-1 peptide and caries risk in a group of Hispanic children by determining (1) Do caries- prone children have low levels of hBD-1? and (2) Do caries-prone populations have SNPs in hBD-1 that are associated with caries risk? In addition, we will determine association of individual SNPs with salivary hBD-1 levels. Our project is an exploratory study designed to foster development of genetic tools as risk factors for varies susceptibility. The risk of caries is highly related to under-served populations and minority ethnic groups, therefore, any new approaches may help in directing attention to the problem and care to those in need.

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- **Project Title: BETA-LACTAMASES AND DD-PEPTIDASES--ACTIVE SITE CHEMISTRY**

  Principal Investigator & Institution: Pratt, Rex F.; Professor; Chemistry; Wesleyan University Middletown, Ct 06459

  Timing: Fiscal Year 2003; Project Start 30-SEP-1982; Project End 31-JAN-2008

  Summary: (provided by applicant): Bacterial resistance to beta -Iactam **antibiotics** continues to become more prevalent and more clinically important. A large part of the resistance can be understood and investigated experimentally in terms of the chemistry of the interactions of a -Iactam **antibiotics** with the active sites of two groups of bacterial enzymes, the beta -Iactamases on one hand, which catalyze the hydrolysis of the **antibiotics,** and the D-alanyI-D-alanine transpeptidase/carboxypeptidases on the other, which catalyze the synthesis and maintenance of the peptide cross-links of bacterial cell walls, and which are inhibited by beta -Iactam **antibiotics.** There is now good reason to

believe that all of these beta -Iactam binding sites have much in common. An understanding of the structure and function of these sites and of the relationship between them is fundamental to future **antibiotics** design - both beta -lactam and otherwise. The object of the proposed research is to explore further the chemical functionality and the substrate binding properties of a series of these active sites, using a number of modified substrates, novel inhibitors and potential effectors. Particular focus will be on the development of ligands, substrate and inhibitors, for the transpeptidases which, to date, have exhibited little in vivo activity except with beta -lactams. This goal will be accomplished by a combination of rational design, combinatorial chemistry, and target-accelerated methods. Crystal structures will be used in conjunction with molecular modeling to interpret the results obtained and apply them to further ligand design. These studies will lead to new insight into the chemistry of beta -Iactamase and transpeptidase active sites, and thus to new directions in **antibiotic** design.

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- **Project Title: BIOACTIVITIES OF PNEUMOCOCCAL CELL WALL IN MENINGITIS**

  Principal Investigator & Institution: Tuomanen, Elaine I.; Chair, Professor; St. Jude Children's Research Hospital Memphis, Tn 381052794

  Timing: Fiscal Year 2001; Project Start 01-JUN-1989; Project End 31-JAN-2005

  Summary: The pneumococcus remains the cause of meningitis with the greatest morbidity and mortality in children and older adults. This pattern persists despite the use of **antibiotics** of exceptionally rapid bactericidal activity. Over the past 10 years of this proposal we have sought to understand the biochemical basis of the inflammatory response to pneumococci in the subarachnoid space. We established that the pneumococcal cell wall is a library of inflammatory components which incites the cytokine, coagulation and arachidonate cascades and directly injures endothelial cells of the blood brain barrier. Further, we established that the release of cell wall during antibiotic-induced death engenders a dramatic host response that is responsible for serious injury to host tissues. This provided a rationale for use of agents like dexamethasone that can act as partner drugs with **antibiotics** to selectively control the injurious components of the host defense response. The current proposal seeks to determine the molecular details of the mechanism of pneumococcal invasion into brain and how neuronal cells are killed during meningitis. Blocking information decreases some sequelae of infection but does not appear to be sufficient in controlling neuronal loss, particularly for pneumococcal disease. Over half of the current survivors of this injection still have major permanent sequelae. Understanding this process will allow design of agents to specifically attenuate these ongoing losses. We propose to apply our expertise in the identification and characterization of pneumococcal surface components, to map the process of transcytosis across the blood brain barrier. We will identify the pneumococcal components involved, specifically focusing on CbpA. This protein is required for pneumococcal invasion. Secondly, we will characterize the process of pneumococcal translocation in terms of the intracellular vesicle and the signaling process. Involvement of the PAF receptor that binds pneumococci and sIgA that ligates CbpA in actual translocation will be determined. Finally, we will investigate preliminary evidence that upon inhibition of apoptosis suggest this is an important contributor to sequelae. The detailed mechanism appears to be novel and will potentially instruct cell biology as well as pathogenesis.

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- **Project Title: BIO-ORGANIC MECHANISMS OF PEPTIDE ANTIBIOTICS**

  Principal Investigator & Institution: Mccafferty, Dewey G.; Assistant Professor; Biochemistry and Biophysics; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2001; Project Start 01-JUN-2000; Project End 31-MAY-2005

  Summary: Bacterial resistance to **antibiotics** has seriously limited our capacity to overcome infectious disease. Cases of resistance have emerged in virtually all hospital-acquired pathogen-antimicrobial combinations. Soon our most serious infectious threats will be untreatable given our dwindling arsenal of effective **antibiotics.** Our long-term research goals are to develop synthetic access to biologically interesting peptide **antibiotics,** to gain insight into their mechanism/mode of action, and to apply the knowledge gained to the development of alternative **antibiotics** with improved activity against resistant phenotypes. This proposal describes the total synthesis and mechanistic characterization of Ramoplanin, a novel beta-sheet lipodepsipeptide **antibiotic** with proven activity against methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus faecium, and cephalosporin-resistant Streptococcus pneumonia, three important Gram positive opportunistic human pathogens. By an unclear mechanism, Ramoplanin appears to arrest bacterial cell wall development at the level of MurG, a glycosyltransferase involved in an intermediate stage of peptidoglycan biosynthesis. Since MurG activity is essential for proper bacterial cell wall development, it is an attractive target for antibacterial design. Harnessing the clinical **antibiotic** potential of Ramoplanin critically hinges on gaining synthetic access to its structure and deconvoluting the most intimate details of its mechanism of action. To accomplish this we will synergistically merge total synthesis, mechanistic enzymology and protein biophysics to completely correlate structure to **antibiotic** function. We plan to synthesize Ramoplanin and related analogues using solid-phase methods, thus providing a general synthetic route to favorably modulate its physiochemical properties. We plan to identify the molecular target of Ramoplanin and determine the interaction energies, specificities, and structure of the inhibitory complex. We will assess the inhibitory effect of Ramoplanin on the MurG reaction and on the mechanistically related peptidoglycan transglycosylation cross-linking reaction that takes place on the outer surface of the bacterial cell membrane. Collectively these studies will provide a clear picture of the mechanism of Ramoplanin inhibition of peptidoglycan biosynthesis and promote the design, synthesis, and biological evaluation of a new generation of **antibiotics** capable of combating bacterial resistance to **antibiotics.**

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- **Project Title: BIOSYNTHESIS OF BETA LACTAM ANTIBIOTICS**

  Principal Investigator & Institution: Townsend, Craig A.; Professor; Chemistry; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2001; Project Start 01-SEP-1978; Project End 31-MAR-2004

  Summary: Penicillin and related beta-lactam **antibiotics** have been a mainstay in the treatment of infections for 50 years. However, their effectiveness, like other known classes of **antibiotics,** has come under increasing challenge from the rise of multiply drug-resistant pathogenic bacteria. Efforts have intensified to understand mechanisms of resistance and to overcome them. Structural modification through genetic manipulation of their biosynthetic pathways is a promising approach to produce variants of known **antibiotics** by cost-effective fermentation and semi-synthetic methods. Continuation of a program to investigate beta-lactam **antibiotic** biosynthesis is

proposed in this application. Three of the four known classes of these **antibiotics** will be studied: (1) clavulanic acid, a potent inhibitor/inactivator of beta-lactamase enzymes and a wide-spread source of resistance, (2) the nocardicins, a family of monocyclic beta-lactams, and the metabolically related monobactams, and (3) the carbapenems, represented clinically by thienamycin and its derivatives, but most simply by carbapen-2-em-3-carboxylic acid. With the recent isolation of biosynthetic gene clusters for at least one member of each of these four principal groups, work is poised to advance rapidly in an integrated research plan using techniques ranging from organic synthesis and enzymology to molecular biology and macromolecular structural methods. Clavaminate synthase will be examined in mutagenesis experiments to identify ligands to the catalytic iron, substrate analogues will be prepared to elucidate the controlling factors in hydroxylation vs. oxidative cyclization chemistry mediated by this protein and as probes in spectroscopic studies of the iron binding site. The newly discovered beta-lactam synthetase active in this pathway will be examined in detail kinetically and for its substrate tolerance, and the poorly understood transformations at the end and beginning of the pathway will be investigated in both gene disruption, and over-expression experiments. The recently discovered nocardicin gene cluster will be studied with emphasis on determining how the presumed precursor peptide is assembled and the beta-lactam formed. Possible evolutionary cross-over between clavulanic acid and the carbpenems will be examined particularly with respect to an apparent similarity of beta-lactam synthesis. These insights will be extended to examination of beta- lactam formation in the prephytotoxin tabtoxin.

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- **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: C.ALBICANS REGULATION BETA-DEFENSINS IN ORAL EPITHELIA**

  Principal Investigator & Institution: Weinberg, Aaron; Associate Professor; Periodontics; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

  Timing: Fiscal Year 2001; Project Start 28-SEP-2000; Project End 31-JUL-2003

  Summary: (adapted from the applicant's abstract) Oropharyngeal candidiasis (OPC) is an emerging disorder owing to the prevalence of AIDS, misuse of **antibiotics,** and host immunosuppression in general. Candida albicans is the most common fungal species isolated from OPC lesions. Recent findings show that mucosal epithelial cells synthesize and secrete antibacterial and antifungal agents, belonging to a family of small, cationic peptides. These molecules, human beta-defensins 1 and 2 (hBD-1, hBD-2) are predicted to function as a first line of host defense against microbial pathogenesis. The PI has discovered that these peptides are expressed in normal human gingival epithelial cells and associated with differentiated epithelium of oral tissues. Moreover, they found that the non oral, yet disseminating isolate C. albicans strain SC5314 stimulates beta-defensin expression in oral epithelial cells, but a clinical OPC isolate does not. This proposal intends to test hypotheses relevant to oropharyngeal candidiasis emanating from the postulate that oral epithelial cells can be stimulated to produce beta-defensins that protect the host from candidal challenges at the oral mucosal barrier. The objectives of this proposal are (1) to determine beta-defensin expression in oral epithelial cells in response to challenge with OPC derived C. albicans isolates, (2) to characterize key virulence factors of C. albicans SC5314 and OPC isolates that lead to beta-defensin response, (3) to examine beta-defensin protection against C. albicans, and (4) to identify genes in oral epithelial cells associated with C. albicans modulation of beta-defensin expression, using microarray technology. The PI hypothesizes that peptide-based antimicrobial defense may be a way in which the gingival epithelium resists invasion of potential pathogens. In light of the frequent adjunctive use of **antibiotics** and antimycotics in treating oral diseases, with the threat of microbial resistance, investigations into novel eukaryotic peptides, such as beta-defensins, are highly significant and offer the potential for future clinical promise. The PI states that this research direction may be significant in leading to future studies with potential application to oral disorders, therapeutic use, and technology development.

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

- **Project Title: CIPROFLOXACIN RESISTANCE AND COMPENSATORY MUTATIONS**

  Principal Investigator & Institution: Adams, Julian P.; Professor; Molecular/Cell/Develop Biology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

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

  Summary: (provided by applicant): The evolution of **antibiotic** resistance in human pathogenic microorganisms is increasingly becoming a serious public health problem. A number of measures have been proposed to combat the spread of **antibiotic** resistance with varying success, including controls of the use of **antibiotics,** the use of vaccines and improvement of hospital hygiene. However, the ultimate success of such measures is questionable, due to evolutionary changes in the resistant sector of the microorganism populations. Many (but not all) mutations to **antibiotic** resistance are deleterious, and therefore may be selected against in the absence of the **antibiotic.** However, under prolonged exposure to **antibiotics,** compensatory mutations can and do occur and be

selected, which reduce the cost associated with **antibiotic** resistance. Such evolutionary changes will contribute to the prevalence to **antibiotic** resistant pathogens, and render some **antibiotics** ineffective. Such a scenario will be particularly disastrous during an anthrax epidemic in this country, for which ciprofloxacin will be the primary **antibiotic** of choice. The principal focus of this project will be to characterize and identify compensatory mutations, which reduce the cost of ciprofloxacin resistance in B. subtilis, a close relative of B. anthracis. The study will also be extended to include E. coli and two other **antibiotics,** novobiocin and ceftazidime. Knowledge of the biochemical and physiological basis of compensatory mutations may allow the design of strategies to reduce or counteract their role in increasing the prevalence of **antibiotic** resistant mutations.

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- **Project Title: COMBATING MULT-DRUG RESISTANT BACTERIA**

  Principal Investigator & Institution: Hergenrother, Paul J.; Chemistry; University of Illinois Urbana-Champaign Henry Administration Bldg Champaign, Il 61820

  Timing: Fiscal Year 2003; Project Start 15-APR-2003; Project End 31-MAR-2008

  Summary: (provided by applicant): Bacterial resistance to **antibiotics** has emerged as a considerable threat to human health. Methicillin-resistant Staphloccous aureus (MRSA) and vancomycin-resistant enterococci (VRE) are multi-drug resistant bacteria that cause life threatening infections in the hospital setting and in some cases have leapt to the larger community. It is clear that new strategies and tactics are needed to combat these insidious bacteria. Often times, bacteria owe their **antibiotic** resistance to the proteins encoded by plasmids that they harbor. Plasmids are small, circular, extra-chromosomal pieces of DNA that can be transferred from one bacterium to another. These plasmids often contain genes that encode proteins that confer resistance to a wide array of **antibiotics.** Indeed, for several classes of **antibiotics** (including beta-lactams, macrolides, and aminoglycosides) plasmid-borne resistance is ubiquitous. In addition, many of the worst multi-drug resistant bacteria (including MRSA and VRE) are resistant by virtue of the plasmid they harbor. Proposed herein is a strategy to attack this plasmid-encoded resistance through the creation of "anti-plasmid" agents, small molecules that will vanquish the plasmid from the cell, thus rendering the bacteria sensitive to **antibiotics.** These compounds are designed to mimic a known, naturally occurring mechanism for plasmid elimination, known as plasmid incompatibility. The bio-molecules that determine plasmid incompatibility are typically small pieces of RNA and DNA iterons. It has been shown that genetic mutation of these RNA incompatibility determinants disrupts RNA loop-loop interactions and leads to plasmid elimination. In Specific Aims 1 and2 of this proposal, small molecules are described that will disrupt the RNA loop-loop interaction in a completely analogous manner, thus leading to plasmid elimination. Specific Aims 3 and 4 describe studies on the mechanism and inhibition of the plasmid replication initiation protein, RepA. The successful completion of the experiments described herein could lead to a dramatic change in the manner in which **antibiotic** resistant infections are treated.

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- **Project Title: CONJUGAL TRANSFER OF BACTEROIDES ANTIBIOTIC RESISTANCES**

  Principal Investigator & Institution: Salyers, Abigail A.; Professor; Microbiology; University of Illinois Urbana-Champaign Henry Administration Bldg Champaign, Il 61820

Timing: Fiscal Year 2001; Project Start 30-SEP-1985; Project End 31-MAY-2006

Summary: (provided by applicant): The incidence of **antibiotic** resistance is increasing in many groups of disease-causing bacteria. Although some bacteria become resistant to **antibiotics** through mutation, acquisition of **antibiotic** resistance genes from other bacteria is probably more common. This proposal focuses on the genus Bacteroides. Bacteroides species are among the numerically predominant species of bacteria in the human colon. Bacteroides species are also opportunistic pathogens that can cause life-threatening infections. Many Bacteroides strains have become resistant to multiple **antibiotics.** Transfer of resistance genes among these strains appears to have occurred mainly through the actions of a group of conjugative transposons (CTns), represented by CTnDOT. CTnDOT excises from the chromosome to form a circular intermediate, which transfers by conjugation to a recipient and integrates into the recipient's chromosome. During the previous funding period, genes responsible for excision and transfer were identified and shown to be controlled by a complex set of regulatory genes. These genes may allow the CTn to coordinate excision and transfer so that nicking to initiate transfer of the circular form does not occur until excision is complete. Both excision and transfer are stimulated over 1,000-fold by the **antibiotic** tetracycline. Previously, we found that three genes, rteA, rteB and rteC function as central regulatory genes. We propose that RteC triggers expression of two excision genes, excA and excB. The first specific aim of the proposal is to test this hypothesis. The second aim is to determine how ExcA and ExcB, presumably in concert with the CTn integrase (Int), catalyze excision and circularization of the CTn. The third specific aim is to determine whether RteC also controls expression of a gene currently designated as orf5 and to test the hypothesis that Orf5 in turn controls the expression of transfer (tra) genes. The fourth specific aim is to answer the question of how effective coordination of excision and transfer actually is. The last aim is to define the characteristics and functions of RteA and RteB, which control expression of rteC.

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- **Project Title: CONTROL OF ARG-2 GENE EXPRESSION IN NEUROSPORA**

  Principal Investigator & Institution: Sachs, Matthew S.; Associate Professor; Environmental and Biomolecular Systems; Oregon Health & Science University Portland, or 972393098

  Timing: Fiscal Year 2002; Project Start 01-MAY-1992; Project End 31-MAY-2006

  Summary: (provided by applicant): The goal of this work is to understand how a peptide encoded by an upstream open reading frame (uORF) controls the movement of ribosomes on mRNA and regulates gene expression. The arginine attenuator peptide (AAP) is encoded by a uORF in mRNAs specifying a fungal arginine (Arg) biosynthetic enzyme and reduces gene expression when Arg is high. AAP-mediated regulation is observed in vitro using extracts from fungi and wheat germ. The nascent AAP causes the ribosome to stall in response to Arg. Stalled ribosomes block access to the downstream start coclon that initiates enzyme synthesis. The AAP is a unique eukaryotic peptide because its synthesis can arrest ribosomes involved in both termination and elongation. Its study provides exceptional opportunities to examine central translational processes that are still not understood. It will provide valuable information on events within the ribosome for evaluating the functions of **antibiotics** that interfere with translation. Since uORFs that control gene expression are found in animals, plants, fungi, viruses and bacteria, the proposed work is directly relevant to understanding these important regulatory elements.In a working model for regulation, the nascent AAP stalls the ribosome by adopting a conformation that, with Arg,

interferes with decoding at the ribosomal A site, or with other steps crucial for translation. The proposed studies will test and refine models for AAP-mediated regulation. Specific aims are: 1. Directly examine the regulatory mechanism by (a) establishing whether stalled ribosomes contain the nascent AAP covalently linked to tRNA to determine whether peptidyl transferase activity is blocked, (b) using photocross-linking of the nascent chain to the ribosome to examine conformational changes in the interaction between the nascent AAP and the ribosome in response to Arg, (c) using photocros s-linking of Arg analogs to determine whether Arg interacts with the AAP or with the translational machinery, and (d) determining whether regulation requires only translational components conserved between prokaryotes and eukaryotes. 2. Examine mutations in nonsense-mediated mRNA decay (NMD) for their effects on mRNA stability and AAP-termination codon recognition. NMD mutations eliminate regulation by the uORF-encoded AAP in vivo. 3. Identify additional trans-acting genes important for translational control by examining mutations in fungi that affect Arg-specific regulation or translation in vivo for their effects on AAP-mediated ribosome stalling in vitro. Cloning and identification of the genes and analysis of their functions should provide a rational explanation of the mutations. 4. Obtain an in-depth understanding of regulatory function by mutational analysis of stalling sites in combination with the use of **antibiotics** affecting translation and trans-acting mutants affecting regulation.

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- **Project Title: CONTROL OF BIOFILMS BY NATURAL PRODUCTS**

  Principal Investigator & Institution: Costerton, John William.; Professor & Director; Sequoia Sciences 11199 Sorrento Valley Rd, Ste H San Diego, Ca 92121

  Timing: Fiscal Year 2003; Project Start 01-APR-2001; Project End 31-JAN-2005

  Summary: (provided by applicant): Chronic bacterial infections are serious medical problems in the United States. In chronic bacterial infections, biofilms protect bacteria from **antibiotics** and immune response mechanisms, thus increasing the rates of reoccurring symptoms and resistance to **antibiotics.** We discovered four novel compounds in Phase I under this STTR project that prevent the formation and disrupt biofilms, and we expect to identify additional novel compounds in Phase II. We propose to use the strategies developed in Phase I to prioritize the other active samples that have been identified. We will elucidate the structures of the active compounds and characterize their biological activity as biofilm inhibitors or antibacterials. We will also continue the discovery process for additional active samples. This work will enable us to commercialize these compounds that regulate biofilms and to further optimize or methods and strategies by which to discover more novel compounds that regulate formation of biofilms that are needed for a wide range of applications. In the United States, the market for microbial biofilm inhibitors is contained within the $8.5 billion market for **antibiotics.** Biofilms are involved in 65% of human bacterial infections; accordingly, biofilm inhibitors could capture a $4 to $6-billion segment of the **antibiotic** market. Biofilm inhibitors will have the greatest medical impact by treating many chronic infections, reducing catheter- and medical device-related infections, and in treating cystic fibrosis patients. Research has clearly established that biofilms play a significant role in these areas, representing a large market whose needs are unmet. The potential market penetration for potent biofilm inhibitors is exemplified by the sheer number of cases in which biofilms cause medical problems.

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- **Project Title: CONTROL OF DNA TOPOLOGY**

  Principal Investigator & Institution: Tse-Dinh, Yuk-Ching; Associate Professor; Biochem and Molecular Biology; New York Medical College Valhalla, Ny 10595

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

  Summary: Due to the recent emergence of pathogenic bacteria resistant to all **antibiotics** currently used, there is an urgent lead to develop new **antibiotics** against novel targets. Bacterial topoisomerase I is a promising new target for antibacterial therapy with lead compounds having MIC's of 4.0 mug against Staphylococcus aureus. E. coli topoisomerase I is the best studied example of bacterial topoisomerase I and share extensive homology with topoisomerase I from both gram-positive and gram- negative bacteria. Topoisomerase I targeting drugs that inhibit DNA religation would lead to cell killing in a mechanism similar to those of many drugs targeting bacterial DNA gyrase and human topoisomerases. Loss of topoisomerase I function may also affect the ability of the bacteria to respond to environmental challenges encountered in pathogenesis. The long term goals of this project include the elucidation of the mechanism, regulation and physiological roles of E. coli topoisomerase I, which would greatly aid the development of novel bacterial agents targeting this class of enzyme. The aims for this proposal include: 1. Structure-function analysis by different mutagenesis approaches to identify residues required for the individual steps of catalysis by E. coli topoisomerase I 2. Limited proteolysis and chemical cleavage of topoisomerase I in the absence and presence of DNA to identify sites of cleavage altered due to either enzyme conformational change or protection by DNA substrate. 3. Test of peptide sequences identified by panning as potential inhibitor of topoisomerase I 4. Study of the molecular basis of topoisomerase I involvement in bacterial adaptation to environmental challenges for survival.

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- **Project Title: CORE--MEDIA PREPARATION FACILITY**

  Principal Investigator & Institution: Barch, David; Northwestern University Office of Sponsored Programs Chicago, Il 60611

  Timing: Fiscal Year 2001; Project Start 01-AUG-1993; Project End 31-JUL-2006

  Summary: (provided by applicant): The Robert H. Lurie Comprehensive Cancer Center?s Media Preparation Facility supports the research of Cancer Center members with reliable low cost centralized media preparation and reagent supply services. To keep users up to date on policies and procedures and to inform them of new products and services, The Media Preparation Facility utilizes an annually printed catalog, bulk e-mail notifications, as well as a facility web site. The Media Preparation Facility has been in operation since 1981 and currently employs one full time laboratory coordinator/supervisor and one lab assistant. The NCI Center Support Grant Review Committee felt that the Media Preparation Facility was a valuable asset of the Cancer Center providing a well organized service at low cost to members. The Media Preparation Facility prepares custom tissue culture media and reagents which would be impossible or too expensive for researchers to purchase from outside vendors. In addition, standard media, **antibiotics,** animal sera, and various reagents are stocked as pass-through items. These items are purchased in such large volumes that the prices are well below those that would be available to

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- **Project Title: CRYSTALLOGRAPHIC STUDIES OF RIBOSOMAL PARTICLES**

  Principal Investigator & Institution: Yonath, Ada E.; Weizmann Institute of Science Box 26 Rehovot, 76100

  Timing: Fiscal Year 2003; Project Start 01-AUG-1985; Project End 31-MAY-2006

  Summary: (provided by applicant): Goals: The long-term goal of our project is to shed light on the molecular mechanism of protein biosynthesis. Ribosomes are the universal cell organelles facilitating the translation of the genetic code into proteins. These nucleoprotein assemblies (mw 2.3 mega-Dalton, about 4500 RNA nucleotides and 75 proteins) are built of two subunits of unequal size (0.85 and 1.45 mega-Dalton), which associate upon the initiation of protein biosynthesis. The immediate objectives of this proposal are (a) to use the high-resolution structures of the two eubacterial ribosomal subunits determined by us as references for the elucidation of the structures of ribosomal complexes with substrate analogs, functional ligands, inhibitors and **antibiotics;** (b) to exploit these structures for illuminating the mechanisms involved in peptide bond formation, decoding, translocation, inhibition by and resistance to **antibiotics;** (c) to progress toward high resolution structure determination of complexes capturing the whole ribosome at defined functional states; (d) to advance towards the determination of the structure of eukaryotic ribosomes. Methods: Highly active ribosomes from robust organisms are being crystallized. X-ray diffraction data are being collected at cryogenic temperatures from flash-frozen crystals, using state-of-the-art high brilliance synchrotron radiation. Phases are being determined by a combination of MIRAS, molecular replacement and crystal averaging, and used to locate the bound ligands and **antibiotics** in difference electron density maps. The significance of ribosomal crystallography stems from its potential to illuminate the mechanism of a fundamental life process, protein biosynthesis. The already known structures revealed the modes of action of several **antibiotic** agents that target the ribosome, illuminated principles of drug selectivity, and provided significant basic knowledge of possible pathways of drug resistance. These, and further to come insights, should lead to improved therapeutic agents and allow structure based design of a new generation of more powerful, selective and efficient **antibiotics.**

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- **Project Title: DEALING WITH ANTIBIOTIC RESISTANCE--ANTISENSE TECHNOLOGY**

  Principal Investigator & Institution: Tolmasky, Marcelo E.; Biological Science; California State University Fullerton 800 N State College Blvd Fullerton, Ca 92631

  Timing: Fiscal Year 2000; Project Start 01-JUN-2000; Project End 31-MAY-2004

  Summary: (Adapted from Applicant's Abstract): Drug resistance is a major obstacle in the conquest of bacterial infections. This proposal targets a critical issue in the treatment of bacterial infectious diseases: the need to develop strategies aimed at preserving the effectiveness of currently available aminoglycoside **antibiotics.** The investigators focus on resistance to the aminoglycoside amikacin mediated by the aminoglycoside 6'-N-acetyltransferase AAC(6')-Ib, which can also modify several other aminoglycoside **antibiotics.** The long term goal of this research project is to develop the use of antisense oligonucleotides as tools to selectively inhibit the expression of aac(6')-Ib and other related genes. The specific aims for this grant proposal are: 1a) Identification of synthetic oligonucleotides and analogs that promote cleavage of aac(6')-Ib mRNA by RNase H or RNase P. 1b) Bioavailability studies of synthetic oligonucleotides and oligonucleotide analogues. RNase H or RNase P can mediate inhibition of gene expression by

degradation of mRNA in the presence of appropriate antisense molecules. The general strategy of this specific aim will consist of the utilization of two conceptually different approaches to identify regions in the mRNA available for interaction with oligonucleotides. With this information, oligodeoxynucleotides and analogues will be designed to inhibit the expression of aac(6')-Ib by inducing RNase H degradation of the mRNA. The information will also be utilized for the development of antisense oligoribonucleotides that inhibit the expression of aac(6')-Ib by inducing RNase P degradation of the mRNA. Following, the investigators will initiate studies on the cell uptake of oligonucleotides and analogues. 2a) Development of peptide nucleic acid (PNA) molecules that inhibit expression of AAC(6')-Ib. 2b) Bioavailability studies of PNA molecules. A novel strategy to inhibit gene expression using antisense technology is now available with the synthesis of peptide nucleic acids (PNAs). PNAs may be developed as antimicrobial agents in prokaryotic systems. The investigators will test the in vitro and in vivo activity of several PNA molecules to interfere with the expression of aac(6')-Ib. The investigators will then study the bioavailability of naked and liposome encapsulated PNA molecules.

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- **Project Title: DEVELOPMENT OF DAM INHIBITORS AS NOVEL ANTIBIOTICS**

  Principal Investigator & Institution: Johnson, Paul H.; Epigenx Pharmaceuticals Pacific Training Center Santa Barbara, Ca 93111

  Timing: Fiscal Year 2003; Project Start 01-JUL-2000; Project End 31-JAN-2005

  Summary: (provided by applicant): The focus of this proposal is to develop drug candidates that inhibit DNA Adenine Methyltransferase (DAM) as a new class of **antibiotics** for the treatment of bacterial infection. Widespread **antibiotic** resistant pathogenic organisms create life-threatening conditions for patients in both hospital and community settings. To deal with increasing drug resistance, new antibacterial agents are desperately needed. We have established purified enzymes and in vitro and in vivo assays for high throughput compound screening, and compound optimization for potency and selectivity. Screening of chemical diversity libraries has identified several new classes of compounds that inhibit bacterial DAM. We will expand the high throughput screening effort initiated in the SBIR Phase I to include assay automation, the screening of additional small molecule template libraries, and the identification and characterization of new lead compounds. Existing lead compounds will be prioritized on the basis of their potential for chemical optimization and mechanism type. Combinatorial and/or focused libraries will be prepared and screened for the most promising template series and structure-activity relationships (SAR) developed. Chemical optimization will be performed with respect to potency, selectivity against mammalian enzymes, in silico and experimental ADME parameters, and uptake by bacterial cells. Potential drug candidates will be evaluated in animal and cell-based model systems for efficacy and toxicity. A wide spectrum of clinically important pathogenic bacteria will be screened for sensitivity to methylation inhibition. The outcome of this 2-year development program will be a drug candidate ready for Phase I clinical evaluation in humans.

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- **Project Title: DEVELOPMENT OF NEW LIPID A BINDING AGENTS**

  Principal Investigator & Institution: Savage, Paul B.; Associate Professor; Chemistry and Biochemistry; Brigham Young University A-261 Asb Provo, Ut 846021231

Timing: Fiscal Year 2001; Project Start 01-JUN-1998; Project End 31-MAY-2003

Summary: Sepsis affects the lives of hundreds of thousands of people each in the U.S. Sepsis caused by Gram-negative bacteria results from adverse host immune response to the Lipid A (LA) portion of endotoxin. Compounds with high affinity for LA, including polymyxin B (PMB) and derivatives, are capable of detoxifying LA nd protection a host against sepsis. By binding LA, these compounds also sensitize Gram-negative bacteria to hydrophobic **antibiotics.** However, therapeutic use of PMB is limited due to its toxicity. The aim of this research is to develop small molecules capable of strong and selective associating with LA for use in treatment of sepsis and as means of fighting bacterial infection. Taking the interactions of PMB with LA as a model, this research focuses on the preparation of simple compounds, based on cholic acid scaffolding, capable of mimicking the LA-binding behavior of PMB but lacking the toxicity of the **antibiotic.** Simple cholic-acid based LA binders will present many advantages over reported LA binding molecules including: ease of preparation and derivatization, greater control over biological stability, and potential oral bioavailablity. Cholic acid derivatives were designed to mimic a conformation of PMB believed to be important in its association with LA. Preliminary experiments with cholic acid derivatives demonstrate their ability to sensitize Gram- negative bacteria to hydrophobic **antibiotics,** a behavior of LA binding agents. Optimization of LA-binding characteristics will be achieved by preparing libraries of compounds made up by amino acids linked to cholic acid scaffold. The libraries will be screened for LA binding using affinity chromatography. The affinity chromatography stationary phase will be made up of LA immobilized through hydrophobic interactions of C18- silica particles or polystyrene beads. The types of amino acids in effective LA binders will be determined via mass spectroscopy. New LA-binding agents will be tested for the ability to sensitize Gram- negative bacteria to hydrophobic **antibiotics** and/or inhibit the effects of LA on human monocytes (specifically interleukin 1b production). Association of PMB and the new LA-binders with LA and LA derivatives will be compared using microtitration calorimetry.

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- **Project Title: DYNAMIC BEHAVIOR OF RIBOSOME LIGANDS DURING TRANSLATION**

  Principal Investigator & Institution: Agrawal, Rajendra K.; Wadsworth Center Empire State Plaza Albany, Ny 12237

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

  Summary: The ribosome is a large complex of ribonucleoproteins, which interacts with several protein factors and RNA molecules to conduct the life sustaining process of protein biosynthesis. It is also the target site of several **antibiotics,** which inhibit specific steps during the interaction of protein factors with the ribosome. Very little is known about molecular details of the dynamic events that take place during this interaction of ribosomes. Very recently, impressive progress has been made towards solving the atomic structure (for example, structures of ribosomal subunits from a thermophilic bacterium and a halophilic archaeon are known to 3 - 2.4 Angstrom units resolution); however, it will take many years before various dynamic events can be trapped and analyzed by X-ray crystallography of the complete ribosome. This proposal describes the development of a method that is uniquely suited to study the dynamic events on the ribosome at near atomic resolution and in close to in vivo condition. We plan to strategically label specific amino acid residues of protein ligands (EF-G, EF-Tu, release and recycling factors) with heavy metal clusters and form a complex with the ribosome. The complex will be imaged by the technique of single particle reconstruction of images

obtained from cryo-electron microscopy (conceived and successfully applied in the laboratory of Dr. Joachim Frank, the co-PI). The resulting density maps will be analyzed in terms of the X-ray structure of the ligand by a flexible docking method. We have preliminary data showing that the technique of labeling of specific amino acid with heavy metal and binding of the heavy-metal-labeled ligand to the ribosome are feasible. Although the approach has broad applications, the main emphasis of this proposal is to understand the molecular basis of the conformational changes of various ribosome-binding factors and their relevance in protein biosynthesis.

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- **Project Title: ENZYMATIC RXN. OF DEOXYSUGARS IN NOVOBIOCIN BIOSYNTHESIS**

  Principal Investigator & Institution: Freel Meyers, Caren L.; Biological Chem & Molecular Pharm; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

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

  Summary: (provided by applicant): The emergence of antibiotic-resistant bacteria has become a critical health concern; hence, the design of new agents which will combat the problem of developing resistance to **antibiotics** is of major interest. The **antibiotic** novobiocin is produced by Streptomyces spheroides and is a part of the aminocoumarin family of **antibiotics** whose mode of action is the inhibition of the type II DNA topoisomerase DNA gyrase. The structure of novobiocin consists of three moieties: a noviose sugar, a 3-substituted coumarin ring and a prenylated 4-hydroxybenzoic acid moiety. It is suggested that the noviose sugar moiety is important for recognition of the target gyrB; therefore, it is of great interest to study the enzymes involved in the biosynthesis and subsequent reactions of the noviose moiety of novobiocin. The focus of this research proprosal is divided into three specific aims: 1) characterization and substrate specificity study of NovM, the putative glycosyltransferase for glycosylation of the novobiocic acid by TDP-noviose 2) characterization and specificity studies of NovP and NovN, the noviose tailoring enzymes in the biosynthesis of novobiocin and 3) the in vitro reconstitution of TDP-noviose biosynthesis. The genes encoding NovT,U,W,S,M,P and N will be cloned from genomic DNA isolated from Streptomyces spheroides, the proteins expressed in E.coli and purified by Ni (II)-affinity chromatography. Characterization of enzyme activity in each case will be accomplished using established assays. NovM, P and N will be assayed for activity with normal and modified mbstrates using established HPLC assays. It is anticipated that these studies will advance the development of biosynthetic combinatorial libraries of sugar-modified novobiocin analogs.

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- **Project Title: ENZYMOLOGY OF ANTIBIOTIC RESISTANCE**

  Principal Investigator & Institution: Armstrong, Richard N.; Professor; Biochemistry; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

  Timing: Fiscal Year 2001; Project Start 01-FEB-1998; Project End 31-JAN-2003

  Summary: Five decades ago the introduction modern **antibiotics** began a revolution in effective therapy for infectious diseases. Today those advances in chemotherapy are in jeopardy due to the increasingly common appearance of drug resistant strains of microorganisms. The treatment of increasing numbers of immunocompromised individuals represents at once a clinical challenge that must be met and a venue for the

selection of new, more resistant strains. It is not clear that enterococci resistant to all major classes of **antibiotics** are an immediate threat in the clinic. Fosfomycin is a potent, broad-spectrum **antibiotic** effective against both Gram-positive and Gram-negative microorganisms. Early in the last decade plasmid-mediated resistance to fosfomycin was observed in the clinic. Subsequent investigations established that the resistance plasmids encode metalloproteins (FosA or FosB) that catalyze the addition of glutathione to the **antibiotic,** rendering it inactive. More recently, chromosomal resistance genes encoding putative fosfomycin canoeists have been described. The objectives of this research project are to elucidate the catalytic mechanisms, and structures of enzymes involved in the resistance of microorganisms to fosfomycin. These objectives include, the construction of high-level expression systems for the proteins, the elucidation of their catalytic mechanisms, and the determination of their three-dimensional structures by X-ray crystallography. The investigations of the fosfomycin resistance proteins FosA and FosB will include: (i) a determination of the kinetic mechanism of catalysis by pre-steady state and steady state kinetic techniques; (ii) elucidation of chemical mechanism of catalysis including the role of the role of the metal ion in the reaction by magnetic resonance (EPR and ENDOR) techniques; (iii) the determination of the enzyme-substrate interactions important in catalysis; and (iv) determination of the three-dimensional structures of the apoenzyme and the holoenzyme with bound Fosfomycin. The specific aims of the project with respect to the fosfomycin kinase FosC include: (i) synthesis if the gene and expression of the protein in E.coli; (ii) a determination of the structure of the product of the enzymatic reaction and an investigation of the kinetic mechanism of the enzyme including the divalent cation requirement; (iii) and examination of the hypothesis that FosC. and another kinase FomA are related and (iv) initiation of X-ray crystallographic investigations of the structure of FosC. It is anticipated that this investigation will establish the mechanistic and structural foundation for design of new drugs to counter resistance to fosfomycin. The project is a response to program announcement PA-97-026, Aspergillosis, Ehrlichioses and Drug Resistance.

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- **Project Title: EXPERIMENTAL MODEL FOR CHORIOAMNIONITIS AND PREMATURITY**

  Principal Investigator & Institution: Gravett, Michael G.; Chief; None; Oregon Health & Science University Portland, or 972393098

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

  Summary: Prematurity is the leading cause of neonatal morbidity and mortality in the United States. Intrauterine infections are an important, and potentially treatable cause of prematurity, and are associated with increased risk of neonatal white matter lesions of the brain and cerebral palsy. However, the mechanisms by which infection leads to prematurity and/or cerebral palsy remain speculative and treatment strategies untested largely because humans cannot be longitudinally studied following infection. We propose to use chronically instrumented pregnant rhesus monkeys at 120-130 day gestation with experimental intrauterine infection, as previously described (Gravett et al, Am J Obstet and Gynecol; 171:1660-1667,1994) to study the temporal and quantitative relationships among infection, cytokines, prostaglandins, steroid hormones, cytokine antagonists, preterm labor, and neonatal white matter lesions of the brain in order to develop effective interventional strategies. After postoperative stabilization in a tether, we will; (1) inoculate Group B Streptococci (GBS) into the amniotic fluid to establish intrauterine infection and preterm labor. Uterine contractility will be continuously

monitored and periodic samples of amniotic fluid and maternal and fetal blood (1-4 cc) will be obtained for assays of eicosanoids, steroid hormones, cytokines, matrix metalloproteinases and for microbial studies; (2) utilize **antibiotics** with and without potent inhibitors of proinflammatory cytokine production (dexamethasone,IL-10) o prostaglandin production (indomethacin) to ascertain the most effective intervention to down-regulate the cytokine/prostaglandin cascade and associated uterine activity; (3) infuse proinflammatory cytokine IL-1beta into the amniotic cavity through indwelling catheters in the absence of infection. Prior to infusion of IL-1beta in the absence of infection, specific novel proinflammatory cytokine inhibitors (IL-1ra and sTNF-R1 PEG) will be used to identify other potentially useful immunomodulators. Samples of the decidua, fetal membranes, tissues, and brain will be obtained at cesarean section for microbiologic, histopathologic studies, immunohistochemistry for cytokines, localization and quantitation of mRNA for cytokines and PGHS-2. Fetal brain will be examined for increased apoptosis associated with white matter lesions. Leukocytes in amniotic fluid and tracheal aspirates will be assessed by flow cytometry Postpartum, the mother will be treated with appropriate **antibiotics** to eradicate the GBS from the genital tract and returned to the colony. These studies will clarify the pathophysiology of infection-associated preterm labor and will suggest effective interventional strategies.

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- **Project Title: FORESPORE ENGULFMENT DURING B. SUBTILIS SPORULATION**

  Principal Investigator & Institution: Pogliano, Kit J.; Biology; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, Ca 92093

  Timing: Fiscal Year 2003; Project Start 01-JAN-1998; Project End 31-DEC-2006

  Summary: (provided by applicant): Bacteria from the genera Bacillus and Clostridium produce unusually durable and long-lived spores that are the infectious agent of Anthrax and Botulism, and which are assembled in the cytoplasm of another cell. This unique cell within a cell structure is produced by the phagocytosis-like process of engulfment, during which the membrane of the larger mother cell migrates around the smaller forespore, until it is completely enclosed within the mother cell cytoplasm. Engulfment provides a dramatic example of the dynamic capabilities of the bacterial cell, but its mechanism remains unclear. Previously, the only engulfment mutants blocked septal thinning, during which peptidoglycan within the septum is thinned in preparation for membrane migration. We have developed new tools for the study of engulfment, and identified mutants defective in membrane migration, and in the final step of engulfment, membrane fusion. The membrane fusion defective mutants affect a protein that is both highly conserved and essential in many species. This protein localizes to site of division and is involved in the final stages of chromosome segregation, suggesting that it may also be involved in membrane fusion at the completion of cell division, a process about which little is known. Sporulation-specific enzymes are required to hydrolyze peptidoglycan during septal thinning, and we will test if vegetative autolysins can partially substitute for the sporulation specific enzymes. Autolysins are found in all bacteria (the Bacillus subtilis genome is predicted encode more than 30such enzymes), and are thought to allow peptidoglycan remodeling for cell elongation and division. However, these enzymes are potentially lethal, since unless they are tightly regulated both spatially and temporally, their activity can result in cell lysis. Indeed, the lethality of many commercial **antibiotics** requires autolysins. Engulfment provides an ideal system for understanding how bacteria control these potentially lethal enzymes, which are attractive targets for novel **antibiotics.** We will take a combined cell biological, genetic and biochemical approach to study the spatial

regulation of peptidoglycan hydrolysis, the mechanism of membrane fusion in bacterial cells, as well as to understand how bacteria move and localize macromolecules within their cells

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- **Project Title: GONOCOCCI: GENETICS OF RESISTANCE TO PMN PROTEINS**

  Principal Investigator & Institution: Shafer, William M.; Professor; Microbiology and Immunology; Emory University 1784 North Decatur Road Atlanta, Ga 30322

  Timing: Fiscal Year 2001; Project Start 01-APR-1984; Project End 31-MAR-2005

  Summary: (Adapted from the application abstract) Neisseria gonorrhoeae is an obligate human pathogen and has the capacity to infect and cause disease at numerous sites. However, this capacity requires that gonococci resist antibacterial substances that naturally bathe mucosal surfaces or become available due to inflammation. The emphasis of this project is to understand the mechanism(s) used by gonococci to resist antibiotic-like substances that bathe certain mucosal sites. The mtr (multiple transferable resistance)and far (fatty acid resistance) loci contain operons that encode efflux pump proteins that export structurally diverse antibacterial hydrophobic agents (HAs), including bile salts, fatty acids, lysosomal proteins and **antibiotics.** The MtrCDE and FarAB proteins belong to families of bacterial proteins that form efflux pumps that remove structurally diverse antimicrobial agents from either the periplasm or cytoplasm. Expression of these efflux pump operons are subject to both negative and positive transcriptional control systems. For instance, the MtrR protein down-regulates expression of the mtrCDE operon through its capacity to bind to the mtrCDE promoter and this results in enhanced susceptibility of gonococci to certain HAs. Conversely, expression of the farAB operon, which encodes an efflux pump that exports long-chained fatty acids with potent antigonococcal activity, seems to be dependent on MtrR. Through the use of modern techniques in microbial genetics, molecular biology and biochemistry, we will determine the mechanisms by which MtrR exerts transcriptional control over these efflux pump operons and other gonococcal genes (Specific Aims I and 3). Expression of the mtrCDE operon can also be induced during exposure of gonococci to sub-lethal levels of HAs. This induction process requires a transcriptional activator, MtrA, that belongs to the AraC/XylS family of DNA-binding proteins. The mechanisms by which MtrA exerts its control over gonococcal gene expression will be determined (Specific Aim 2). Dr. Shafer'sins group has recently identified a novel protein (MtrF) that seems to act as a component of the mtrCDE-encoded efflux pump. MtrF counterparts exist in several other bacteria but their function has yet to be determined. Given its apparent wide-spread distribution, they will determine its role in efflux. pump activity (Specific Aim 4). The results from these studies will advance our knowledge regarding how gonococci and other pathogens resist antimicrobial agents at mucosal surfaces, **antibiotics** used in therapy of bacterial diseases, and topical microbicides that have been proposed for use to prevent sexually transmitted diseases.

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- **Project Title: GRANULYSIN DERIVED IMMUNOTHERAPEUTICS FOR BIODEFENSE**

  Principal Investigator & Institution: Clayberger, Carol A.; Associate Professor; Pediatrics; Stanford University Stanford, Ca 94305

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

Summary: (provided by applicant): Defense against infections related to the use of biological agents in acts of terrorism or war is a national priority. To achieve this end, new methods to detect, treat, and prevent infection with Category A-C pathogens must be developed. Treatment may include prevention of infection in the case of an immediate threat, protection of immunocompromised individuals, or post-exposure treatment to suppress infection and disease. Ideal agents for these applications would be stable, broad spectrum, fast acting, nontoxic towards human cells, inexpensive, and easy to manufacture. Conventional **antibiotics** meet some of these criteria, but both the rise in **antibiotic** resistant organisms and a dearth of new broad-based **antibiotics** make identification of new antimicrobials imperative. Granulysin is an alpha-helical protein expressed by human natural killer cells and activated T lymphocytes. Recombinant granulysin lyses both mammalian cells and a broad spectrum of microbes. Synthetic peptides (10-30 residues) corresponding to the central region of granulysin recapitulate its lytic activity. In a subset of these peptides, replacement of cysteine or arginine residues, or introduction of D-amino acids to disrupt the alpha-helix, results in the loss of activity against mammalian cells with little or no effect on antimicrobial activity. The goal of this Program is to develop novel immunotherapeutics based on these granulysin peptides. Additional derivatives will be generated in Project 1, evaluated in vitro and in vivo in Project 2, and characterized for mechanism of action in Project 3. These projects will be supported by three cores--synthesis/inventory; a BSL-3 facility, and administration. The information gleaned from these studies should lead to the development of new immunotherapeutics for biodefense and for treatment of **antibiotic** resistant pathogens.

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- **Project Title: HUMAN DENDRITIC CELLS AND IN VIVO IMMUNITY TO BIOTHREAT**

  Principal Investigator & Institution: Banchereau, Jacques F.; Director; Baylor Research Institute 3434 Live Oak St, Ste 125 Dallas, Tx 75204

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

  Summary: (provided by applicant): Vaccines and **antibiotics** permitted to combat many infectious diseases. While a wealth of vaccines has been developed, natural evolution and engineering for bioterrorism purposes creates a novel biothreat for which novel vaccines are needed. Dendritic cells (DCs) play a central role in the differentiation of immune effectors and thus are a major target for vaccination. Given the fact that distinct human DC subsets differentially control lymphocytes, it is important to understand how distinct DC subsets modulate vaccine immunity in vivo. Such knowledge will permit us to design targeted vaccines that will induce a desired type of immunity. Vaccines need to be tested in vivo but studies in mice often cannot be directly extrapolated to humans because of biological differences. Hence, the need for pre-clinical models of the human immune system for testing vaccine efficacy. With this in mind, The goal of the Center is to develop effective diagnostic, prognostic, and therapeutic measures against NIAID Category A-C pathogens through a focus on human dendritic cell subsets, which act as innate effectors as well as initiators and coordinators of adaptive immune responses. Objectives: 1. Develop our in vivo model of human immune responses based on mice reconstituted with a full human immune system. 2. Generate novel monoclonal antibodies identifying i) the various human DC subsets at their various stages of maturation, and ii) peptides derived from biothreat antigens presented by dendritic cells 3. Determine how Category A-C pathogens alter human dendritic cells in vitro and in vivo. 4. Determine the effects of Category A-C pathogens on the human immune system

in vivo. 5. Identify the in vivo biosignatures of human Category A-C pathogens to allow rapid biothreat diagnosis, prediction of disease severity and initiation of biothreat specific treatment. 6. Test and identify in vivo novel human vaccines as biothreat countermeasures. The Program will include a Technical Development Component, four projects, 3 Core facilities: Administration, Microarray and Luminex multiplex analysis, and Education component. Two pilot projects are also proposed. Center will be based at the Baylor Institute for Immunology Research at Dallas and will include Investigators at Yale U., Rockefeller U., NIAID, U. of New Mexico and UT Southwestern. By harnessing human DC subsets in vivo we surmise that we will able to propose novel potent vaccines to protect humans against category A-C pathogens.

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- **Project Title: IN VIVO MODELS OF DEFENSIN ACTIVITY**

  Principal Investigator & Institution: Bevins, Charles L.; Associate Staff; Cleveland Clinic Foundation 9500 Euclid Ave Cleveland, Oh 44195

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

  Summary: (provided by applicant): The discovery of antimicrobial peptides in insects, lower vertebrates and mammals has unveiled a previously unrecognized component of animal host defense. Antimicrobial peptides are gene-encoded **antibiotics** with activity against many classes of microbes. Defensins are the predominant family of such peptides in mammals. Studies by our group and others have discovered that defensin peptides are expressed by mammalian mucosal epithelial cells, providing them with the capacity to participate in local host defense. Although the intestinal epithelium is a surface in continual contact with luminal contents variably laden with microbes, infection is uncommon. Our underlying hypothesis is that in humans, the epithelial defensins HD5 and HD6 contribute to antimicrobial defense of the enteric mucosa. In this grant proposal, we will test biological functions of epithelial antimicrobial peptides in vivo through transgenic expression of HD5 and HD6 peptides in mice. We propose that transgenic expression of these human defensins may provide mice with an enhanced capacity to resist bacterial challenges. Based on preliminary studies of our established transgenic mice, the experiments described here will establish a clearer understanding of the contributions of human antimicrobial peptides to innate host defense. To test our hypotheses, Aim 1 will assay the immunological consequences of human HD5 expression in transgenic mice. We will characterize the ability of HD5 transgenic mice, compared to control wild-type mice, to resist enteric infection by Salmonella typhimurium (Aim 1A), and parallel experiments will extend to other enteric pathogens (Aim 1B). We will examine the impact of transgenic HD5 expression on resident microflora of the mouse intestine (Aim 1C). The antimicrobial activity contributed by transgenic expression will be quantitated in vitro, including analysis of isolated crypts (Aim 1D). The HD6 gene and peptide share little sequence identity to HD5, yet they are expressed together in Paneth cells. In Aim 2, we will generate HD6 transgenic mice (Aim 2A) use recombinant HD6 to develop an antibody for immunoassays (Aim 2B), and characterize the transgenic expression of HD6 at the gene and protein level (Aim 2C). We will then characterize the effects of transgenic HD6 expression on resistance to enteric bacterial colonization and infection (Aim 2D) using the approaches developed in Aim 1. Finally, through lineage interbreeding we will create HD5/HD6 compound transgenic mice to determine if these two peptides have synergistic activities in vivo (Aim 2E). The proposed investigations, and other studies of innate immunity, may provide insights yielding novel therapeutic targets and approaches to combat infectious disease.

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- **Project Title: INNATE IMMUNITY AND MYOCARDIAL INJURY**

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

  Timing: Fiscal Year 2002; Project Start 05-FEB-2000; Project End 31-JAN-2004

  Summary: Both humans and experimental animals with heart failure exhibit increased expression in the heart of inflammatory cytokines, including TNF, IL-1beta and IL-6, as well as iNOS, in the absence of evidence of infection. While maladaptive cardiac remodeling has been attributed to these proteins, the proximal events that trigger and sustain their expression are not well understood. Each of these mediators, however, are now known to be related to innate immunity, an evolutionarily ancient arm of the immune system that is triggered by pattern recognition receptors (PRRs), such as the toll-like receptors (TLRs) expressed by invertebrates and vertebrates, that recognize largely invariant structural motifs on pathogens. It is now recognized that innate immune PRRs also may have evolved in eukaryotes to recognize and repair or remove injured or dying cells, again by recognizing relatively invariant motifs found on injured cells or on cells programmed to die. Based on these observations and our own preliminary data, we hypothesize that vertebrate TLR4, which is expressed by cardiac myocytes, plays a pivotal role in the response to injury in the heart. Specifically, we will examine: 1) the regulation of TLR4 expression in cardiac myocytes in vitro in response to injury induced by UV light, by anthracycline **antibiotics** and by cyclic biaxial strain coupled with electric field pacing, as well as in cardiac myocytes in situ in remodeling murine ventricular muscle following experimental myocardial infarction; 2) the signal transduction pathways leading to NFkappaB and MAP kinase activation by activated TLR4 in cardiac myocytes and their possible localization to caveolar microdomains; and 3) the functional role(s) of TLR4 in the response to myocyte injury in vitro and in vivo; specifically, we will test the hypothesis that: i) a constitutively activated TLR4 construct conveys a survival signal in vitro; ii) that TLR4 participates in the recognition and removal of apoptotic cells; and iii) that animals with targeted disruption of TLR4, or of its immediate downstream signaling target MyD88, exhibit altered rates of ventricular remodeling in response to myocardial infarction.

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- **Project Title: MECHANISM OF KDO 8-P AND DAH 7-P SYNTHASE**

  Principal Investigator & Institution: Woodard, Ronald W.; Professor; Medicinal Chemistry; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

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

  Summary: (Provided by Applicant) Health care providers are challenged daily by an increasing resistance of pathogenic bacteria to their antibacterial arsenal. To overcome this problem, it is necessary to design new and innovative **antibiotics** with totally different modes of action so that, no cross-resistance with present agents should occur. Most antimicrobial drugs act by inhibiting key enzymes in the biosynthesis of macromolecular molecules necessary for viability of the microorganism. Success in this type of approach necessitates a thorough understanding of the enzyme(s) at the molecular level. The goal of this work is to collect mechanistic information on the enzymes 3-deoxy-D-mannoo-octulosonate 8-phosphate and 3-deoxy-D-arabino-heptulosonate 7-phosphate synthase. The information will prove useful in the design of

selective inhibitors of these unique enzymes, namely a new generation of mechanistically diverse **antibiotics.** The goals of this project are to establish 1. The mechanism for the formation of 3-deoxy-D-manno-octulosonic 8-phosphate (KDO 8-P) from arabinose 5-phosphate (A 5-P) and phosphoenolpyruvate (PEP) catalyzed by the enzyme KDO 8-P synthase (EC 4.1.2. 16), an enzyme involved in the biosynthesis of the lipid A portion of the lipopolysaccharide region of the cell envelope of gram-negative bacteria, 2. The mechanism for the formation 3-deoxy-D-arabino-heptulosonate 7-phosphate (DAH 7-P) from erythrose 4-phosphate (E 4-P) and PEP catalyzed by the enzyme DAH 7-P synthase [EC 4.1.2.15], the enzyme that catalyzes the first committed step in the biosynthesis the aromatic amino acids and various aromatic secondary metabolites. The specific alms focus on the use of diverse techniques to "visualize" the potential tetrahedral intermediate. These methods include a rapid mixing, pulsed-flow ESIMS technique to confirm the formation of a reaction intermediate(s) and rotational-echo double-resonance NMR experiments of sub-zero substrate entrapped in enzyme to observe the intermediate. A rapid temperature quench methodology will be developed to isolate the potential intermediate(s) for NMR structural studies. Multinuclear NMR analysis of the interaction of the synthases with various labeled substrate analogues will be utilized to observe abortive intermediates and substrate analogs designed to "stabilize" this potential abortive intermediate(s) will be used to further understand the mechanisms of these reactions. The role of the metal ion will also be investigated. Site-directed mutagenesis studies, based on x-ray crystallographic data, will be exploited to gain further insight into the contribution of enzyme functionalities to substrate binding, monomer interface interactions and to the mechanism of the enzyme.

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- **Project Title: MECHANISM OF STAPHYLOCOAGULASE-ACTIVATED BLOOD CLOTTING**

  Principal Investigator & Institution: Bock, Paul E.; Associate Professor; Pathology; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

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

  Summary: (provided by applicant): The broad goal of the proposed studies is to define the molecular mechanism of the activation of human blood coagulation by the S. aureus protein, staphylocoagulase (SC), and the role of the mechanism in the pathogenesis of endocarditis. SC binds tightly to human prothrombin (Pro) and induces formation of a functional catalytic site in the zymogen without the usual strictly required peptide bond cleavages. This unique conformational activation mechanism is hypothesized to involve initial encounter of SC and Pro, followed by activation of the catalytic site and occupation of regulatory proexosite I in two or more discrete conformational changes. The mechanism may involve conformational linkage between proexosite I occupation and catalytic site activation, stabilization by high affinity binding of SC to the active conformation, and is unlikely to require insertion of the SC amino-terminus into a binding pocket in the Pro catalytic domain. The mechanism underlying the unique specificity of SC-Pro to convert fibrinogen (Fbg) to fibrin (Fbn) is hypothesized to bypass and inhibit the normal reactions of Pro activation. This mechanism is central to the propagation of platelet- Fbn-bacteria vegetations on heart valves in endocarditis. Fbg clofting activity of the SC-Pro/T complexes is hypothesized to involve specific recognition of Fbg as a substrate through expression of a Fbg-binding exosite on the SC-Pro/T complexes, in addition to changes in catalytic site specificity. Biochemical, biophysical, and structural approaches employing novel active site-labeled fluorescent derivatives of Pro are proposed to test hypotheses for conformational activation of Pro

by SC and the basis of its specificity for conversion of Fbg to Fbn. Specific Aims are: (1) To determine the thermodynamic mechanism of conformational activation of Pro by SC; (2) To define the kinetic pathway of individual molecular events in conformational activation; (3) To elucidate the mechanism of specific recognition of Fbg as a substrate of SC-Pro/T complexes; and (4) To determine the three dimensional structures of SCI-327 bound to Pro/T species. The proposed studies are of fundamental significance in understanding how SC can circumvent the otherwise strict requirement for peptide bond cleavage in serine proteinase zymogen activation. The studies will provide new insight into the role of activation of Pro by SC in the pathogenesis of endocarditis and may ultimately allow therapy adjunctive to **antibiotics** to be developed based on inhibition of SC-activated blood coagulation.

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- **Project Title: MECHANISMS OF ANTIBIOTIC EFFLUX IN CAMPYLOBACTER**

  Principal Investigator & Institution: Zhang, Qijing; Vet Microbiol & Prev Medicine; Iowa State University of Science & Tech Ames, Ia 500112207

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2006

  Summary: (provided by applicant): Campylobacter jejuni, an important foodborne pathogen causing gastroenteritis in humans, has evolved multiple mechanisms to counteract the action of various **antibiotics,** which has posed a serious threat to public health, Many of these resistance mechanisms, such as gyrA mutations and beta-lactamase production, confer Campylobacter resistance to specific **antibiotics.** However, the active efflux systems, which extrude structurally diverse **antibiotics** out of bacterial cells, contribute to the intrinsic and acquired resistance to multiple drugs. Although previous studies suggested the possible presence of functional efflux systems m C. jejuni, the **antibiotic** efflux machinery in this pathogen has not been defined. Using transposon mutagenesis in conjunction with other approaches, we have recently characterized a three-gene operon (named cmeABC) encoding a tripartite **antibiotic** efflux pump that contributes to C. jejuni resistance to structurally unrelated **antibiotics,** heavy metals, bile salts, and other toxic compounds. Our preliminary data and the genomic sequence of C. jejuni NCTC 11168 suggested the presence of an additional **antibiotic** efflux system (name cmeDEF) and the possible regulation of cmeABC and cmeDEF by transcriptional repressors. Based on these observations and the known features of bacterial **antibiotic** efflux systems, we hypothesize that CmeDEF in conjunction with CmeABC plays an important role in extruding various agents, and the modulated expression of the efflux pumps by regulatory proteins contributes significantly to the intrinsic and acquired resistance of Campylobacter to multiple antimicrobials. To test our hypothesis, we plan to i) determine the role of CmeDEF and its interplay with CmeABC in mediating Campylobacter resistance to multiple drugs and ii) to identify and characterize the transcriptional repressors that modulate the expression of the **antibiotic** efflux systems. Various genetic and biochemical approaches, including random and site-specific mutagenesis, recombinant proteins, substrate accumulation assay, and DNA binding assays will be utilized to define the functions of the efflux systems and their interplay with regulatory proteins. It is anticipated that the proposed studies will close a major gap in our understanding of the **antibiotic** resistance mechanisms in C. jejuni and may open new avenues for the design of effective means to prevent and treat antibiotics-resistant Campylobacter.

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- **Project Title: MECHANISMS OF BIOFILM ANTIBIOTIC RESISTANCE**

  Principal Investigator & Institution: O'toole, George A.; Assistant Professor; Microbiology and Immunology; Dartmouth College 11 Rope Ferry Rd. #6210 Hanover, Nh 03755

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

  Summary: (provided by applicant): Biofilms are complex bacterial communities attached to a surface. The formation of biofilms has a profound impact on human health and industrial processes and has been recognized as an important, but poorly studied aspect of the bacterial life cycle, Biofilm development includes a transition from individual, planktonic (free-swimming) bacteria to a mode of life attached to a surface as part of a multi-cellular community, and the subsequent return to a planktonic existence. One of the most widely recognized properties of bacteria growing in a biofilm is their increased resistance to antimicrobial agents. Despite increasing interest in understanding how resistance develops, little is known about the molecular mechanisms that drive biofilms cells towards this highly resistant state. Our evidence supports the central hypothesis of this proposal: antimicrobial resistance of biofilm-grown cells requires distinct genetic elements. Herein, we propose a series of complimentary approaches to elucidate molecular mechanisms underlying biofilm-specific **antibiotic** resistance using three model **antibiotics.** While part of the proposed work will continue our efforts to study known biofilm-specific functions in P. aeruginosa (Specific Aim I), work described in Specific Aims II and III will begin in depth analysis of two newly discovered genetic loci required for resistance to **antibiotics** in a biofilm. The multiple experimental approaches outlined in this proposal should lead to a better understanding of the mechanism(s) involved in development of biofilm-specific **antibiotic** resistance, and potentially to new therapeutic strategies for modulating these properties. Specific Aim I. Studies of known genes in biofilm-specific **antibiotic** resistance. Specific Aim II. Determine the role of a glucan synthetase enzyme in the development of biofilm-specific **antibiotic** resistance. Specific Aim III. Studies of the role of a putative new efflux pump in biofilm-specific **antibiotic** resistance.

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- **Project Title: MECHANISTIC STUDIES ON PEP UTILIZING ENZYMES**

  Principal Investigator & Institution: Anderson, Karen S.; Professor; Pharmacology; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

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

  Summary: (adapted from applicant's abstract): Phosphoenol pyruvate (PEP) is a highly functionalized, chemically versatile molecule involved at several intersections of cellular energy metabolism and biosynthesis. While most enzymatic reactions utilizing PEP as a substrate involve cleavage of the high energy P-O, two types of reactions have been shown to involve the unusual cleavage of the C-O bond of PEP. These enzyme reactions fall in to two classes: (1) the first class is those that carry out an enolpyruvoyl transferase reaction and (2) the second class are those that carry out what is formally a net aldol condensation reaction. Representative enzymes in the enolpyruvoyl transferase class include EPSP synthase and MurZ. To date, there are only two known enzymes that carry out the net aldol condensation between PEP and the aldehyde moiety of a cosubstrate sugar: KDO8P synthase and DAHP synthase. Recently, a third enzyme, N-acetyl-neuraminic acid synthase, has been discovered that also appears to fall in to this category. Each of these bacterial enzymes is responsible for catalyzing the formation of key components such as lipopolysaccharide, aromatic amino acids, and capsular

polysaccharides that are found in unique biosynthetic pathways and therefore may represent novel target enzymes for the design of new **antibiotics.** While the mechanistic aspects of the catalytic pathway for the enolpyruvoyl transferase have been delineated, the details of the catalytic mechanism for those enzymes in the second class that are involved in the net aldol condensation remain elusive. This proposal will investigate the catalytic mechanism for each of the three enzymes that catalyze a net aldol condensation and define the second class of enzyme that cleave the C-O bond of PEP. The two specific aims of this proposal are: 1) Elucidation of the KDO8P synthase molecular mechanism using transient kinetic methods to study: a) structure guided site-directed enzyme mutants and b) a series of alternate substrate and reaction intermediate analogs; and 2) Detection and characterization of novel enzyme intermediate from a series of three PEP-utilizing enzymes using a novel rapid mixing, pulsed-flow ESI-MS technique. These enzymes carry out a unique aldol type condensation of PEP and sugars of increasing length: C4 (DAHP synthase), C5 (KDO8P synthase), and C-6 (N-acetyl-neuraminic acid synthase). In addition as the investigator develops the quantitative aspects of the rapid mixing, pulsed-flow ESI-MS technique further, she will extend the studies of these enzymes to determine the full kinetic profile.

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- **Project Title: MECHNANISM OF TRANSCRIPT ELONGATION CONTROL BY RFAH**

  Principal Investigator & Institution: Artsimovitch, Irina; Microbiology; Ohio State University 1800 Cannon Dr, Rm 1210 Columbus, Oh 43210

  Timing: Fiscal Year 2003; Project Start 01-FEB-2003; Project End 31-JAN-2008

  Summary: (provided by applicant): Expression of many genes is limited by the ability of RNA polymerase to complete polymerization of up to a million nucleotides, making elongation to emerge next to initiation as a major regulatory step in gene expression. Several accessory protein factors that allow RNA polymerase to overcome this limitation and become "elongation-proficient have been described. The focus of this proposal, the bacterial protein RfaH, is a regulator of several long virulence and fertility operons, where it preferentially increases the expression of distal genes. We have demonstrated that RfaH binds to its recruitment sequence, ops, exposed on the surface of the RNA polymerase paused at an ops site during elongation. Following its recruitment, RfaH stimulates transcription downstream of an ops site by enhancing elongation rate and suppressing pausing. However, RfaH only modestly inhibits termination. The detailed mechanism of RfaH action, described as "antitermination', remains obscure except for the fact that it is different from those of other antiterminators such as lambdaN and lambdaQ, which have profound effects on both elongation and termination. Both the recruitment mode and the effect of RfaH on elongation are unique, thus insights into the RfaH mechanism will contribute to the general understanding of the regulation of transcript elongation in bacteria and also in eukaryotes, where RfaH homologs are implicated in elongation control and localize to the actively transcribed sites. In this proposal, we will use a combination of biochemical, genetic, and biophysical approaches to address several aspects of RfaH action. The first goal of this project is to elucidate the molecular mechanism by which RfaH affects elongation thousands of nucleotides downstream of its recruitment site. The central mechanistic question to be answered is whether RfaH travels with the elongating RNA polymerase or if it causes a conformational change in the RNA polymerase that persists for thousands of nucleotide addition steps after RfaH dissociates from the complex. The second goal of this project is to determine how universal is this mechanism by finding out whether RfaH affects

transcription similarly at all sites or is targeted to a particular set of regulatory signals. The third goal of this project is to map interactions between RfaH and the transcription elongation complex, thus placing RfaH mechanism in its structural context. RfaH controls the expression of the secreted molecules, components of the cell wall, **antibiotics,** virulence factors, and proteins required for the mobilization of transmissible plasmids. Proposed studies will therefore positively impact research in several areas of bacterial biology and evolution, such as synthesis of extracytoplasmic components, bacterial virulence, lateral gene transfer, and emergence of pathogens.

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- **Project Title: METAL ION PROBES MEMBRANE PROTEIN STRUCTURE AND FUNCTION**

  Principal Investigator & Institution: Bowman, Michael K.; Staff Scientist; Battelle Pacific Northwest Laboratories Box 999, 902 Battelle Blvd Richland, Wa 99352

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

  Summary: (provided by applicant) The focus of this proposal is to understand the basis for the specific structure/function relationship in complex protein reactions by examining differences and similarities between the 'same' protein from different organisms. This approach will help to understand the natural variation in protein structure, function and other properties between different isoforms or different species and is a necessary complement to the study of site-directed mutants of a single protein. This effort is part of a long-term interest in the use of EPR as a structural probe and draws on experience in developing and applying innovative EPR methods for answering specific biological and physical questions. This work will provide insights into the bioenergetically important cytochrome bc-type complex and the metabolically important eukaryotic cytochrome P450 enzymes that could lead to new, highly-selective drugs and **antibiotics** exploiting differences between these proteins in different organisms or between different isoforms in humans. The methods developed in carrying out this work will be broadly applicable to other membrane proteins and other protein complexes.

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

- **Project Title: METTALLOENZYME STRUCTURE/FUNCTION**

  Principal Investigator & Institution: Merz, Kenneth M.; Professor; Chemistry; Pennsylvania State University-Univ Park 201 Old Main University Park, Pa 16802

  Timing: Fiscal Year 2002; Project Start 01-APR-1991; Project End 31-MAR-2006

  Summary: The long-term goal of this research is to understand, at the molecular level, the catalytic mechanism and inhibition of beta-lactamases and through this understanding facilitate the development of small-molecule therapeutics. Bacterial resistance to beta-lactam **antibiotics** has emerged over the past decade as a major health concern. Beta-lactam **antibiotics** kill bacteria by preventing the complete synthesis of the bacterial cell wall leading to a defective cell wall, which ruptures under the high internal pressure of the cell. Bacteria have developed antibiotic- resistance strategies in three major ways: production of hydrolytic enzymes known as beta-lactamases, changes in the permeability of the cell membrane, and alterations of the target enzymes. Among these mechanisms, beta-lactamase production, relentlessly fueled by natural selection, is generally considered as the primary route of resistance to beta-lactam **antibiotics.** Significantly, these enzymes can be chromosome or plasmid encoded and are secreted into the periplasmic space of Gram- negative bacteria or into the outer medium by

Gram-positive bacteria, which facilitates the spread of beta-lactam resistance. The emerg3ence of anti-beta-lactam activity also has a tremendous social and financial impact because of the continuous need to discover novel **antibiotics.** The tools that will be used to reach the long-term goal are those of theoretical chemistry, medicinal chemistry and biochemistry. The primary enzymes that will be studied are the beta-lactamases from B. cereus and B. Fragilis. With the aid of these tools the nature and energetics of beta-lactamase-substrate interactions, beta-lactamase- inhibitor interactions and reactions catalyzed by these beta-lactamases will be examined. The insights obtained into these processes will have a major impact on human health by facilitating the design of new drugs that will eliminate at least one bacterial mechanism for anti-beta-lactam activity, which will in turn increase the lifetime of existing **antibiotics.**

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

- **Project Title: MOLECULAR EVOLUTION OF ENTERIC BACTERIOCINS**

  Principal Investigator & Institution: Riley, Margaret A.; Associate Professor; Ecology and Evolutionary Biol; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

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

  Summary: Microbes are engaged in a never-ending arms race. This microbial warfare is directed in large part at conspecifics and close relatives with which they compete most intensively for access to niches and nutritional resources. One evolutionary consequence of this intense competition is the diversity of antimicrobial compounds that most species of bacteria produce. Surprisingly, there has been little attention paid to understanding either the role these compounds play in natural microbial communities or their evolution. One class of antimicrobials, the bacteriocins, has received increasing attention because of the surprisingly high levels of bacteriocin diversity observed, the widespread distribution of bacteriocins in bacteria, and the use of bacteriocins as preservatives in the food industry and as **antibiotics** in the human health industry. We now have a sophisticated understanding of the molecular mechanisms involved in bacteriocin-mediated killing, cell recognition and transport into the cell. However, very little effort has been focused on addressing ecological and evolutionary questions, such as: what role do these toxins play in mediating microbial interactions, what are the origins of and evolutionary relationships among this heterogeneous class of proteins, what molecular mechanisms are involved in their diversification, and what are the evolutionary responses to such an arsenal of weapons, i.e. the mechanisms of defense and the resulting evolutionary arms race? The focus of this research proposal is to specifically tackle these issues. We propose to provide a detailed description of the frequency and distribution of bacteriocin production and resistance in one clinically relevant, division of bacteria, the Enterobacteriaceae. Novel bacteriocins will then be cloned and sequenced. These data will help us to determine the phylogenetic range over which bacteriocins act, the levels of naturally occurring resistance, as well as determine the evolutionary relationships among enteric bacteriocins and their modes of diversification. In essence, what we propose is to explore the natural history of bacteriocins in search of a better understanding of how bacteriocins, and other related antimicrobials, can be used to replace, or supplement, classical **antibiotics.** The understanding that we gain regarding the natural role of bacteriocins, and the defenses raised against them within bacterial communities, can be directly applied to the rational application of novels antimicrobials to human health issues

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

- **Project Title: MOLECULAR GENETICS AND MECHANISM OF PROTEIN ANTIBIOTICS**

  Principal Investigator & Institution: Hansen, J Norman.; Professor; Chemistry and Biochemistry; University of Maryland College Pk Campus College Park, Md 20742

  Timing: Fiscal Year 2001; Project Start 01-APR-1987; Project End 31-MAR-2003

  Summary: Certain strains of Bacillus subtilis produce subtilin, which is a broad-spectrum ribosomally-synthesized **antibiotic** peptide that contains many unusual amino acids (dehydroalanine, dehydrobutyrine, lanthionine, beta- methyllanthionine) as a consequence of posttranslational modifications of serine, threonine and cysteine residues present in the precursor peptide. Recent studies in this laboratory have used site-directed mutagenesis of the subtilin prepeptide gene to construct and express a structural analog of subtilin, in which the change of a single amino-acid residue resulted in dramatic enhancement of its chemical and antimicrobial properties. This proves the potential of using a genetic engineering approach to the design and construction of improved and novel **antibiotics** that may have expanded therapeutic potential with respect their natural forms. Because of the malleability of protein structures, it is realistic to hope that these analogs could be targeted to a variety of infectious agents, perhaps even including viruses. The purpose of this project is to increase our understanding of how to use mutagenesis for structure-function studies by acquiring fundamental information about the mechanism by which the cellular machinery recognizes the subtilin precursor peptide, the steps in the biosynthetic pathway, and the involvement of the prepeptide leader sequence in maturation and secretion. Because the natural producer of subtilin is an uncharacterized strain, the capability to produce subtilin was transformed into B. subtilis 168, for which an enormous amount of genetic information is available. We have exploited the well-established genetic tools available for strain 168 to construct and express mutant genes in which the subtilin leader region (has no normal secretion signal) is fused to PhoA as a reporter. Expression of fusion showed that the leader region directs secretion of the PhoA reporter through a secretion pathway that exists only in the subtilin-producing mutant of 168; but not in wild-type 168. This implies that subtilin-producing cells have a novel and uncharacterized secretion system that specifically recognizes the subtilin leader sequence. The secretion apparatus may also contain the enzymes that catalyze the post-translational modifications. This will be explored by examining the fusion proteins for the presence of the unusual amino acid residues, using a combination of N-terminal sequence, total amino acid composition, and NMR-spectroscopy. A variety of fusion proteins will be constructed for the purpose of localizing the recognition signals in the precursor peptide as being in the leader region, the mature region, or distributed throughout the peptide. Site-directed mutagenesis of the unusual amino acids will be used to explore their roles in the chemical properties and the **antibiotic** mechanism of subtilin. Finally, we will determine whether the five ORFs that have been identified in the spa operon are the only genes required to support subtilin biosynthesis, and if not, locate and identify any additional genes. The roles of the ORFs will be explored by mutating them one at a time using in-frame deletions, and inferring the role of each ORF in the biosythetic pathway by determining which step in the pathway is interrupted by each mutation.

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- **Project Title: MOLECULAR MECHANISMS OF MEMBRANE TRANSPORT**

  Principal Investigator & Institution: Cafiso, David S.; Professor; Chemistry; University of Virginia Charlottesville Box 400195 Charlottesville, Va 22904

  Timing: Fiscal Year 2001; Project Start 06-SEP-1985; Project End 31-JUL-2004

Summary: Active and passive transport are critical process for normal cell metabolism, including the maintenance of ion-gradients, osmotic balance, membrane potentials, and apoptosis. In spite of their widespread importance, the molecular mechanisms that lead to transport have not been characterized, which is in part due to the difficulty associated with obtaining structural information on membrane proteins. The work that is described in this proposal is directed at investigating the mechanisms of action of two transport systems. BtuB is an outer membrane transport protein for vitamin B12 found in gram negative bacteria, and it obtains its energy for transport by coupling to the inner membrane protein TonB. Using site-directed spin-labeling and EPR spectroscopy, we will test proposals for the molecular mechanisms of transport in BtuB. This class of membrane proteins is of fundamental interest because it is the only class of membrane active transport proteins for which high-resolution structural models have been obtained; as a result, they are likely to be the first active transport systems for which detailed molecular mechanisms will be obtained. In addition to the accumulation of nutrients, this class of proteins functions in the uptake of bactericidal agents, such as colicins, phages and small molecule **antibiotics.** The widespread importance of these TonB dependent systems for bacterial function makes them probable targets for the development of new classes of **antibiotics.** A second system that will be studied is alamethicin, a peptide **antibiotic** that forms voltage-dependent ion channels in bilayers. Voltage- dependent events in membrane proteins are also of widespread importance, but have not been characterized at a molecular level. Alamethicin belongs to a larger class of membrane active peptides having important **antibiotic,** fungicidal, hemolytic and tumoricidal activities. In addition to its voltage-dependence, alamethicin has received attention because it appears to be selective towards certain organisms. In the work proposed here we will develop a method to apply electric fields across vesicle and supported bilayers and will use NMR, EPR and FTIR to test mechanisms for the voltage-dependence in this peptide. We will also test mechanisms that could account for the selectivity of this **antibiotic** against certain membranes.

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- **Project Title: MOLECULAR ROLE OF 16S RIBOSOMAL RNA IN TRANSLOCATION**

  Principal Investigator & Institution: Joseph, Simpson; Chemistry and Biochemistry; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, Ca 92093

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

  Summary: (provided by applicant): Protein synthesis is a fundamental process in all living organisms. Ribosomes are the ribonucleoprotein complexes responsible for protein synthesis. Recent atomic resolution structures of the large and small ribosomal subunits provide a unique opportunity to understand the mechanism by which ribosomes perform the complex task of protein synthesis. One of the important steps in the elongation cycle of protein synthesis is the iterative movement of the tRNA-mRNA complex, a process called translocation. In Escherichia coli, elongation factor G (EF-G) catalyzes translocation. The mechanism of EF-G-dependent translocation is poorly understood. The long-term goal of my laboratory is to elucidate the molecular basis of translocation. Several lines of studies indicate that the ribosomal RNAs (rRNAs) may play a functional role during translocation. We recently developed a novel modification-interference approach that will permit us to examine the role of 16S rRNA in translocation. The method uses a highly efficient site-specific cross-link between P site bound tRNA and 16S rRNA to select ribosomes that are active in translocation. We will use a combinatorial approach for identifying bases, non-bridging phosphate oxygens,

and ribose 2'-hydroxyl groups within 16S rRNA that are critical for translocation. This study will provide information about the dynamics of ribosome structure that cannot be easily acquired by X-ray crystallography. Ribosomes are the target for inactivation by several classes of **antibiotics. Antibiotics** such as eiythromycin, spectionmycin, viomycin, thiostrepton, and the aminoglycosides specifically inhibit translocation. Some of these **antibiotics** prevent the 16S rRNA from undergoing structural changes that are critical for translocation. Antibiotic-resistant strains of bacteria are on the rise, causing a crisis in the management and treatment of these infections throughout the world. Understanding the mechanism of translocation will provide insights for developing more effective **antibiotics** that target the ribosome of these drug-resistant strains of bacteria.

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- **Project Title: MOLECULAR TARGETS IN PEPTIDOGLYCAN SYNTHESIS**

  Principal Investigator & Institution: Davies, Christopher; Assistant Professor; Biochem and Molecular Biology; Medical University of South Carolina 171 Ashley Ave Charleston, Sc 29425

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

  Summary: (provided by applicant): The murein sacculus is a mesh of cross-linked peptidoglycan strands that confers rigidity to the bacterial cell wall. Beta-lactam **antibiotics,** which target the essential transpeptidases (penicillin-binding proteins or PBPs) that cross-link the peptidoglycan strands, are important compounds in the treatment of bacterial diseases. Unfortunately, the emergence of multiple mechanisms of **antibiotic** resistance threatens to make these and other **antibiotics** obsolete in the treatment of bacterial infections. Along with other pathogenic bacteria, **antibiotic** resistance in Neisseria gonorrhoeae is a growing problem. Penicillin and tetracycline, once the **antibiotics** of choice for treatment of gonococcal infections, are no longer be used due to the emergence of resistant strains. Moreover, increasing numbers of strains are now resistant to the fluoroquinolones, one of the two **antibiotics** current recommended in the treatment of gonorrhea. Clearly there is an urgent need to develop new antimicrobials directed both against well-known molecular targets, such as PBPs, but also against novel targets. In this proposal we describe structural and biochemical studies of three enzymes involved in peptidoglycan metabolism: a D-D-carboxypeptidase from E. coli (PBP 5) that serves as a model system for elucidating PBP function, an essential transpeptidase (PBP 2) from N. gonorrhoeae that is the lethal target of current beta-lactam **antibiotics,** and a lytic transglycosylase, MltA, also from N. gonorrhoeae, that serves as the lynchpin of the cell wall synthesizing complex. Each of these proteins has been selected to address one or more of the following aims: (a) to understand the biology of peptidoglycan synthesis, (b) to explore their interactions with **antibiotics,** (c) to elucidate the molecular basis for **antibiotic** resistance and (d) to examine their potential as targets for drug development. Studies on PBP 5 will elucidate the mechanism by which this enzyme hydrolyzes substrate and will provide a better understanding of PBP-antibiotic interactions in general. The molecular basis for **antibiotic** resistance in PBP 2 will be investigated by structural studies of the native enzyme and of a mutant isolated from a penicillin-resistant strain. The role of MltA as part of a multienzyme complex mediating peptidoglycan synthesis as well as its suitability as a novel target for antimicrobials will be examined by solving its crystal structure. These studies will provide a framework for future studies aimed at structure-based drug design and will provide substantial insight into the mechanisms of peptidoglycan synthesis.

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- **Project Title: MYCOTHIOL BIOSYNTHESIS AND METABOLISM AS TB DRUG TARGETS**

  Principal Investigator & Institution: Fahey, Robert C.; Chemistry and Biochemistry; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, Ca 92093

  Timing: Fiscal Year 2003; Project Start 01-AUG-2000; Project End 31-JUL-2004

  Summary: (provided by applicant): Tuberculosis is now second behind AIDS, as the World's most deadly microbial infection. However, a major fraction of AIDS patients die of mycobacterial infections, including TB. The TB problem is aggravated by the growing prevalence of drug-resistant TB, and especially multi-drug resistant (MDR) TB which cannot be treated with the front-line **antibiotics** for Mycobacterium tuberculosis. It is therefore important that targets be identified for development of new drugs for treatment of MDR TB. Suitable target enzymes should have biochemical functions essential for mycobacteria but with no similar function in mammals making it likely that drugs can be developed that will not lead to adverse reactions in humans. They should have well-defined assays suitable for screening of potential drugs. The proposed research elucidates the biochemistry associated with the production and utilization of the antioxidant thiol known as mycothiol. Mycothiol is produced only by mycobacteria, and other actinomycetes, and is not found in animals. The key genes for mycothiol biosynthesis have recently been identified and provide important potential new drug targets. Studies of MSH-deficient mutants indicate that mycothiol metabolism is involved in protecting against oxidative damage and in the detoxification of **antibiotics,** including one first-line TB drug. Although not essential for the laboratory culture of the model organism Mycobacterium smegmatis, current evidence suggests that mycothiol may be required for survival of M. tuberculosis in an oxygen rich environment. The present studies will determine the extent to which mycothiol is essential for survival of M. tuberculosis, will define the biochemistry involved in the first key step of mycothiol biosynthesis, and will determine how the biosynthesis of mycothiol is regulated. Methods used include new analytical and enzyme assays developed in these laboratories as well as established protocols in biochemistry and molecular biology. The results obtained will provide a key test of the suitability of mycothiol biosynthesis as a target for new TB drugs and will elaborate the biochemistry of a novel class of thiol important to a broad class of soil microorganisms, including most **antibiotic** producing bacteria.

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- **Project Title: NEW KETOLIDE ANTIBACTERIAL DRUGS**

  Principal Investigator & Institution: Hutchinson, Charles R.; Edward Leete Professor; Kosan Biosciences 3832 Bay Center Pl Hayward, Ca 94545

  Timing: Fiscal Year 2002; Project Start 15-FEB-2002; Project End 31-MAY-2003

  Summary: LONG TERM GOAL: Production of novel ketolide **antibiotics** with potent antibacterial activity against macrolide susceptible and resistant bacterial pathogens. PHASE I: We will develop a biological process for production of 15-methyl-6-deoxyerythronolide B, the precursor of 15-methylerythromycin A, through genetic engineering of the 6-deoxyerythronolide B polyketide synthase. This will be accomplished by optimizing the biosynthetic pathway of a substrate used to make the target compound in Streptomyces coelicor, a related actinomycete strain of Escherichia coli. That substrate will be used by an engineered 6-deoxyerythronolide B polyketide

synthase to make 15-methyl-6-deoxyerythronolide B, which will be isolated and bioconverted to 15-methylerythromycins by a strain of Saccharopolyspora erythraea or directly to this compound by an engineered strain of Streptomyces fradiae that contains the genes for production of 15-methyl-deoxyerythronolide B and the 15-methylerythromycins. PHASE II: This process will be optimized for large scale production of 15- methyerythromycins that will be used to make ketolide **antibiotics** in sufficient amount for preclinical and clinical development. Kosan has discovered a lead ketolide in partnership with The R.W. Johnson Pharmaceutical Research Institute and expects that this compound or a close analog will be developed into a drug that is competitive with the two current front runners in this area. PROPOSED COMMERCIAL APPLICATIONS: There is a growing need to discover and develop noel **antibiotics** that can overcome resistance mechanisms. The proposed research will generate modified macrolide **antibiotics** which are effective against macrolide resistant organisms. Since world-wide sales of macrolide **antibiotics** exceed $3B per year, these new **antibiotics** should have significant commercial value.

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- **Project Title: NON ANTIBIOTIC PROPERTIES OF TETRACYCLINE**

  Principal Investigator & Institution: Lokeshwar, Balakrishna L.; Associate Professor; Gordon Research Conferences Box 984, 512 Liberty Ln West Kingston, Ri 02892

  Timing: Fiscal Year 2001; Project Start 19-JUN-2001; Project End 31-MAY-2002

  Summary: This application is a request for supplemental support for a multidisciplinary conference entitled "Non-Antibiotic Properties of Tetracyclines and Other Antibiotics" to be held at Colby Sawyer College, New London, CT during the week of July 1-6, 2001. This meeting held under the auspices of the Gordon Research Conference Society will be the second of its kind on a unique and exciting topic, covering both basic and clinical applications of a class of tetracycline derived compounds and other **antibiotics.** Since first reported in1983 by Golub et al., the non-antibiotic properties of tetracyclines (TCs) and chemically modified non-antimicrobial tetracyclines (CMTs) have found applications in diverse areas of biomedical research. These include: activity as an inducer of tet-on and tet-off gene constructs for in vivo and in vitro gene expression studies, treatment of periodontal disease (Periostat FDA approved 1998), a potential treatment for cancer, arthritis, acute respiratory distress syndrome (ARDS), Sjogrens syndrome and other dry eye diseases, and as an early treatment for stroke. All these applications are based on the anti-metalloproteinase (MMP) and anti-inflammatory properties of TCs. Previous meetings on this novel topic have generated in the biomedical community such immense interest that an overwhelming 80% of the previous attendees have responded with their desire to attend the upcoming meeting. A roster of scientists from the US and Europe, both established workers and those new to the field, have agreed to present and share their recent work on the non-antibiotic properties of TCs and other **antibiotics** and their application to the treatment of disease. The conference will focus on the exchange of new information regarding promising biological models of TC investigation, the molecular mechanism of action and the pharmacology of TCs with an emphasis on cancer, in 8 intensive talk and discussion sessions plus five after session gatherings. The conference is expected to have a significant impact on this rapidly emerging field by fostering collaborations and establishing a forum for discussion regarding the direction of future research.

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

- **Project Title: NOVEL ANTIBIOTICS AGAINST GRAM-NEGATIVE BACTERIA**

  Principal Investigator & Institution: Sweetnam, Paul M.; Surface Logix, Inc. 50 Soldiers Field Pl Boston, Ma 02135

  Timing: Fiscal Year 2003; Project Start 15-AUG-2003; Project End 31-JUL-2005

  Summary: (provided by applicant): Gram-negative bacteria are a major cause of natural outbreaks of disease and feature prominently in the biological arsenals of rogue nations. Compounding this problem is the fact that bacteria are becoming increasingly resistant to current therapeutics, reducing the ability of today's **antibiotics** to treat the victims of natural outbreaks or attacks from engineered pathogens. We propose to target LpxK, an essential kinase involved in the biosynthetic pathway of Lipid A, a major constituent of the gram-negative outer membrane, as a means to develop novel compounds that can prevent or treat bacterial infections with gram-negative bacteria. Innovative surface-based assays will be used to screen compounds against LpxK. Once promising lead compounds are identified, we will perform iterative rounds of medicinal chemistry, optimizing their ability to block enzymatic modification, their efficacy on a variety of bacteria and their pharmacokinetic properties.

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

- **Project Title: NUCLEIC ACID PROBES OF RIBOSOMAL STRUCTURE AND FUNCTION**

  Principal Investigator & Institution: Cooperman, Barry S.; Professor; Chemistry; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2001; Project Start 01-AUG-1995; Project End 31-MAR-2004

  Summary: The ribosome is the unique site of protein biosynthesis in all cells, and as such a detailed understanding of its structure and function is of fundamental importance to the more general understanding of cellular function at the molecular level. Aside from its intrinsic importance to the basic comprehension of life processes, better understanding of ribosomal function could have important therapeutic consequences. Many **antibiotics** in current clinical use, such as tetracycline, erythromycin and other macrolides, neomycin and other aminoglycosides, and chloramphenicol target ribosomes as their sites of action. Interest in these ribosomal **antibiotics** has been growing as bacterial resistance to beta-lactams and quinolines has become more widespread. Several drug companies are now devoting considerable resources toward synthesizing analogues and derivatives of ribosomal **antibiotics** that overcome bacterial resistance. Better understanding of ribosomal structure and function will be especially important for **antibiotics,** such as macrolides, where resistance is based on changes in ribosome structure. Our studies will be carried out on the E. coli ribosome, which is by far the best characterized by the studies of many groups, including our own. However, given the considerable conservation of ribosome structure throughout evolution the results we obtain should also be useful for understanding ribosomes from other organisms. The overall goal of this proposal is to describe conformational changes that the ribosome undergoes during specific steps of its functional cycle and how mutations and **antibiotic** binding affect these changes. We propose to do this by forming defined photocrosslinks from rRNA sites within the ribosome that have been targeted on the basis of their importance for ribosome structure and function, taking advantage of the intrinsic ability of the photocrosslinking process to sample all conformations in solution. Such crosslinks will be formed in different functional states, in wild-type and mutant ribosomes, and in the presence and absence of **antibiotics.** The structural constraints represented by such crosslinks, along with

constraints generated by other approaches, will be used to model structures of the ribosome in specific functional states, using crystal structures of 70S ribosomes and 30S and SOS subunits as initial structures. As our major approach we will continue and refine the use of radioactive, photolabile derivatives of oligonucleotides having sequences complementary to rRNA sequences (PHONTs). Such probes bind to their targeted sequences in intact ribosomal subunits, and, on photolysis, incorporate into neighboring ribosomal components that can subsequently be identified. We also will develop a second approach based on site-specific introduction of photolability into intact rRNA (IPHOR - intact photolabile RNA) to obtain similar information for rRNA sites that are either inaccessible to PHONTs or where the use of PHONTs induces major conformational change.

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- **Project Title: OCULAR PATHOGENESIS AND THERAPY OF BACTERIAL KERATITIS**

  Principal Investigator & Institution: Hill, James M.; Professor; Ophthalmology; Louisiana State Univ Hsc New Orleans New Orleans, La 70112

  Timing: Fiscal Year 2001; Project Start 01-FEB-1991; Project End 31-JAN-2003

  Summary: (from abstract) Bacterial keratitis caused by Pseudomonas aeruginosa is a severe ocular infection that can progress rapidly, resulting in intense ocular inflammation, irreversible stromal scarring of the cornea, blindness, and the need for corneal transplantation. The objective of this project is to improve our understanding of both the bacterial factors and the host immune and nonimmune factors that contribute to stromal damage, as a basis for the development of a chemotherapeutic regimen that prevents corneal scarring. Although intense **antibiotic** therapy of Pseudomonas keratitis kills the bacteria and sterilizes the cornea, damage still occurs; scarring results from a sequence of cellular changes mediated by an inflammatory response in the host cornea. Thus, any therapy, to be clinically successful, must inhibit both bacterial and host factors. Therefore, the specific aims are to test hypotheses concerning the nature of and the contributions of host factors and bacterial factors to corneal inflammation and tissue damage, as well as the mechanisms that must be controlled to reduce scarring. Proposed experiments, both in vitro and in vivo, will 1) define the pathogenic role of bacterial exoproteins in the host tissues, especially proteases; 2) assess combination chemotherapy of keratitis using **antibiotics** to limit production of bacteria and nonsteroidal anti-inflammatory drugs (NSAID) to inhibit inflammation-mediated stromal damage; 3) evaluate protease inhibitors as chemotherapeutic agents to reduce the ability of bacterial and host proteases to mediate tissue damage; and 4) test new chemotherapeutic regimens using **antibiotics** in various combinations that include NSAIDs, steroids, and protease inhibitors in order to simultaneously inhibit both host and bacterial factors. Methods include the use of wild-type Pseudomonas strains compared to exoprotein-deficient Pseudomonas strains in order to identify the specific proteins that produce corneal damage, and the use of recently identified Pseudomonas proteases in order to identify and test appropriate protease inhibitors.

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

- **Project Title: PENICILLIN-RESISTANT NEISSERIA GONORRHOEAE (CMRNG)**

  Principal Investigator & Institution: Nicholas, Robert A.; Pharmacology; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, Nc 27599

  Timing: Fiscal Year 2001; Project Start 01-APR-1996; Project End 31-MAY-2006

Summary: Antibiotic resistance in Neisseria gonorrhoeae remains a very important problem. Penicillin and tetracycline, which were once the **antibiotics** of choice for treatment of gonococcal infections, are no longer used due to the preponderance of strains resistant to these agents. Resistance to currently recommended **antibiotics** is also increasing. My laboratory is interested in the mechanisms of chromosomally-mediated **antibiotic** resistance in the gonococcus, especially those that promote high- level resistance and subsequent treatment failure. Intermediate- level chromosomally-mediated resistance to penicillin and tetracycline is due to three resistance loci. These include the penA gene encoding altered forms of penicillin-binding protein 2 (PBP 2), the mtr loci conferring resistance to hydrophobic agents, and the penB gene, which decreases outer membrane permeability. The genes involved in mediating high-level penicillin resistance, however, have been difficult to identify. Our work during the last funding period has identified two resistance genes, ponA and penC, which together mediate high- level penicillin resistance, and a third gene, tetGC, which confers high-level tetracycline resistance. This proposal outlines experiments to clone and characterize the penC and tetGC genes and to elucidate the mechanisms by which they increase resistance. In addition, we propose experiments that follow up on our structure/function studies of the penB gene product, porin IB, to understand how mutations in this protein increase both penicillin and tetracycline resistance. We also propose studies to complete our work on the crystal structure of penicillin- binding protein 2 (PBP 2), an essential penicillin target, and several mutant forms that display a lower affinity for beta- lactam **antibiotics.** In addition, we will engage in new structural studies of wild-type and mutant forms of porin IB to explicate in molecular detail how mutations in this protein decrease **antibiotic** permeability. The combination of genetic, biochemical, biophysical, and structural approaches outlined in this proposal will provide important insight into the mechanisms by which this important human pathogen becomes resistant to **antibiotics.**

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- **Project Title: PHARMACODYNAMICS IN ANTIFUNGAL RESISTANCE**

  Principal Investigator & Institution: Andes, David R.; Medicine; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

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

  Summary: (provided by applicant): The research performed in the context of the K08 follows work as a fellow and by combining pharmocodynamics (PD) and molecular biology will open the development of an entirely untapped field of study. C. albicans is the most common opportunistic pathogen in HIV infected patients. Azoles are frontline agents for treatment of Candida infections, however therapy remains suboptimal and several mechanisms of azole resistance have recently emerged. There is a need for improved therapy and an understanding of drug exposure factors that lead to and prevent of the emergence of resistance. The proposed research is divided into two phases. (l) In phase one, azole PDs will be studied in a murine model. The findings obtained in the PD studies will be used to optimize dosing of azoles and investigate the relationship between the emergence of specific resistance mechanisms and azole dosing using (a) reconstruction experiments with a susceptible parent strain, doped with a fixed level of the genetically related resistant mutant strain and (b) a strain which has demonstrated temporary phenotypic resistance. (2) In phase two, basic studies of gene expression in C. albicans will be undertaken and correlated with results of phase I PD studies. Serial analysis of gene expression (SAGE) will be used to study mRNA abundance in C. albicans on a genome-wide basis. The biologic variables will include:

the adaptive response of C. albicans to azole **antibiotics** (a) during the initial exposure, (b) following exposure during period of inhibition and regrowth, or the postantifungal effect (PAFE), and (c) the effect of specific known resistance mutations on these responses. The candidate's goal is to integrate knowledge of antifungal PD and the acquisition of approaches and skills in molecular biology through the completion of this grant.

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

- **Project Title: PREVENTION OF BIOFILMS IN MEDICAL DEVICES**

  Principal Investigator & Institution: Shenoy, Bhami C.; Altus Biologics, Inc. 625 Putnam Ave Cambridge, Ma 021394807

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

  Summary: (provided by applicant): Design of new efficient drug delivery systems for proteins is one of the major themes of modern biotechnology and biopharmaceutical industry. We found that cross-linked enzyme crystals (CLECs) show remarkable stability at various pHs, on storage, against proteolysis and organic solvents. These properties make them ideal for treatment against biofilm formation on medical devices /implants such as urethral catheters, ureteric and prostatic stents, penile and testicular implants, artificial urinary sphincters, prostheses for hip and knee replacements, shunts for hydrocephalus, vascular grafts, heart valves, vascular access devices, voice prostheses, etc. In addition, the CLECS can be used for the prevention of blood clot formation, for example, in venous catheters. The CLEC agent will be used to coat the medical devices for the prevention of formation of bacterial biofilms on these devices as well as the prevention of blood clots. The biofilms form on the above medical devices by colonization of bacteria embedded in a matrix, which become resistant to commonly used **antibiotics.** In this Phase I study, we propose to develop two prototypes of CLECs of enzyme - Serratiopeptidase and Streptokinase for prevention of biofilms by Pseudomonas aeruginosa and Staphylococcus aureus microorganisms. The coating will prevent the adherence of these bacteria to medical devices. Currently, there are more than 850,000 case infections associated with aid devices annually in the United States. These may be associated with as many as 100,000 deaths per year. The CLECs of Serratiopeptidase and Streptokinase have enormous commercial potential over the currently available treatment for the prevention of contamination of medical devices by minimizing the need for replacement once they are implanted. The CLECs of Serratiopeptidase and Streptokinase will also be important in preventing biofilm-related infections which are resistant to commercially available **antibiotics.**

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

- **Project Title: RATIONAL DESIGN OF INHIBITORS OF YERSINIA PESTIS EF-TU**

  Principal Investigator & Institution: Totrov, Maxim; Principal Scientist; Molsoft, Llc 3366 N Torrey Pines Ct, Ste 300 San Diego, Ca 92037

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

  Summary: (provided by investigator): The lack of reliable wide-spectrum **antibiotics** and rapid emergence of **antibiotic** resistance in dangerous pathogens poses immediate threats for human health generally and major biodefense concerns. Novel classes of antimicrobial compounds uncompromised by resistance and targeting highly conserved, functionally critical molecular sites in bacteria are urgently needed. Elongation Factor Tu (EF-Tu) is an optimal target for broadly reactive antimicrobials: EF-Tu has at least three functionally relevant binding pockets essentially identical

among many bacterial species, including E. coli, S. typhimurium and S. flexneri, V. cholerae, and plague agent Yersinia Pestis. Recently solved by Dr. Frances Jurnak, UC-Irvine, the 3D structures of EF-Tu protein co-crystallized with natural **antibiotics** explain the atomic details of inhibitor activity of these molecules and provide a solid basis for rational design of new, safe and effective antimicrobials. Our application combines Dr. Jurnak's structural studies with Molsoft's state of the art flexible docking and virtual ligand screening capabilities, and Chemical Diversity Laboratories' expertise in parallel synthesis, biochemical and biological assays to discover new **antibiotics** in a rapid, structure-focused manner.

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- **Project Title: RIBOSOMAL FUNCTION & ANTIBIOTIC DESIGN**

  Principal Investigator & Institution: Mobashery, Shahriar; Professor; Biochem and Molecular Biology; Wayne State University 656 W. Kirby Detroit, Mi 48202

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

  Summary: (provided by applicant): The recent availability of several x-ray crystal structures for the ribosome have created considerable excitement in the field. These structures will be instrumental in devising experiments to elucidate the details of ribosomal synthesis of proteins. Furthermore, the bacterial ribosome is the target of many classes of **antibiotics,** each of which interferes with an aspect of the biochemistry of protein synthesis. Studies of ribosome structures will lead the way in developing novel classes of **antibiotics** in the near future. The long-term goal of this multidisciplinary collaborative project is to utilize the structural information from known x-ray structures to study ribosome function in greater detail and to develop novel inhibitors of an essential and universal biosynthetic process. Four specific aims are proposed. 1) A combination of molecular dynamics simulations and experiments will be used to explore the dynamic nature of the decoding process during peptide-bond formation and to understand the role of **antibiotic** binding in this process. 2) Two molecules that have been designed to explore the motion of the rRNA A site during the decoding process will be synthesized and studied for rRNA binding. These compounds are potential inhibitors of A site function, hence possible antibacterials. 3) Two iron complexes of aminoglycoside-EDTA complexes will be synthesized and tested for their ability to bind the ribosome and fragment the rRNA backbone at sites located within the antibiotic-binding site(s). These experiments will identify the locations in which these **antibiotics** bind, as well as provide information about dynamics through examination of cleavage patterns. 4) Specific aim 4 expands on earlier success in the design of new **antibiotics.** A series of molecules that will interfere with protein synthesis by binding to the ribosomal A site will be generated. A host of specific analyses (assessment of antibacterial properties with living bacteria, translation assays, bacterial membrane permeability assay, assays for DNA and RNA function in bacteria, cytotoxicity assays, assays with A-site mutated 30S ribosomes and bacteria that harbor them, and x-ray analyses of the 30S ribosome and the A-site model complexed with the novel antibiotics) have been envisioned for the study of the antibacterial properties of these molecules. This collective effort will shed light both on the various molecular events within the ribosomal and on how to inhibit some of these processes.

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

- **Project Title: RIBOSOMAL RNA STRUCTURE AND INTERACTIONS**

  Principal Investigator & Institution: Draper, David E.; Professor; Chemistry; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

Timing: Fiscal Year 2001; Project Start 01-APR-1981; Project End 31-MAR-2001

Summary: The long term goal of this project has been to explore molecular interactions in RNA-protein complexes from the ribosome and relate those properties to the functional role of the complex within the ribosome. The results from these studies are anticipated to define, in structural and thermodynamic terms, novel aspects of RNA tertiary structure, the ways in which ligands recognize and manipulate an RNA structure, and the relationship between these interactions and the function of the protein-RNA complex as part of the ribosome. The present work will focus on the interactions of a highly conserved, 58 nucleotide domain of the large subunit ribosomal RNA with a conserved protein, L11, and **antibiotics;** in particular, a hypothesis that the protein binds rRNA in two different modes, both relevant to ribosome function, will be tested. Three kinds of work will be carried out: (1) Structural studies of different protein fragment- and antibiotic-RNA complexes, using "footprint" studies of both protein and RNA, as fragments and in situ in the ribosome, and also using NMR to define the protein and RNA structures and ligand - RNA contact surfaces. (2) Thermodynamic description of L11, L11 fragment, and **antibiotic** binding to rRNA, including the specific uptake of Mg2+ and NH4+ ions. Calorimetry and gel assays will be used to measure binding affinities and associated enthalpies and heat capacity changes. (3) Functional studies of L11 and **antibiotics** in the intact ribosome, starting with the effects of these ligands on elongation factor-G dependent GTPase activity. Results from these studies should contribute to a basic understanding of protein - RNA recognition mechanisms, as well as elucidation of the structure and function of a highly conserved region of the ribosome.

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- **Project Title: RIBOSOME COMPLEXES WITH ANTIBIOTICS AND MACROMOLECULES**

  Principal Investigator & Institution: Moore, Peter B.; Professor; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2001; Project Start 01-APR-1976; Project End 31-MAR-2006

  Summary: The mechanism of ribosome-catalyzed, messenger RNA-directed protein synthesis is fundamentally the same in all organisms, and it is important that it be fully understood for many reasons. First, protein synthesis is a major metabolic activity in all organisms. Second, novel RNA-dependent enzymology may be involved. Third, because so many **antibiotics** target bacterial ribosomes, an understanding of the details of the ribosomal phase of translation may have significant clinical implications. Since lack of atomic resolution information about ribosome conformation has serious limited progress in this area of inquiry for many years. The focus of the work proposed here is the determination of the structure of the ribosome and the complexes it forms with **antibiotics** and the macromolecules with which it interacts by X-ray crystallography. Four projects will be undertaken all in collaboration with R.A. Steitz to a greater or lesser extent. First, the effort to solve crystal structure of the large ribosomal subunit from Haloarcula marismortui, which is already well underway, will be brought to a conclusion. The crystals available diffract past A resolution, and interpretable electron density maps of the structure can be computed today to 5 A resolution. Second, crystals will be prepared of domains of the small ribosomal subunit, in hopes of obtaining information about the conformation of that subunit at resolutions significantly higher than those accessible using the crystals of intact small subunits currently available. Third, a program will be instituted the objectives of which is the determination of the crystal structures of isolated proteins from the large ribosomal subunit of H.

marismortui, or of other archael species, to facilitate the interpretation of the electron density maps of the H. maris mortui 50 ribosomal subunit that are becoming available. Fourth, crystals will be prepared of ribosomes from eukaryotic species, with the ribosomes form yeast being the first objective.

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- **Project Title: RNA POLYMERASE SIGMA SUBUNIT--STRUCTURE AND FUNCTION**

  Principal Investigator & Institution: Burgess, Richard R.; Professor; Oncology; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2001; Project Start 01-DEC-1980; Project End 31-MAR-2005

  Summary: This application proposes to extend detailed studies of the E. coli RNA polymerase major sigma subunit (sigma-70), the interaction of sigma-70 with the core polymerase subunit beta prime, and the competition of various members of the sigma family for binding to core. Specifically, the aims are: To study the interaction of core polymerase subunit beta prime with sigma-70. We have recently developed a powerful new method (ordered fragment ladder far-Western analysis) for mapping protein-protein interaction domains and have used it to map a major binding site for sigma-70 to the amino acid 260-309 region of the beta prime subunit. We will continue these studies to determine the precise nature of this interaction of beta prime 260-309 region of the beta prime subunit. We will continue mutagenesis studies and determine the structure of beta prime 260-309 by NMR in the presence and absence of sigma-70. We will determine where on sigma-70 this interaction is occurring and test the hypothesis that homologous regions of other sigma family members interact with this same site on beta prime. To study competition of sigma-family members for core. We have overproduced and purified all seven E. coli sigmas and have developed immunological reagents and methods to accurately quantitate them. We will measure the binding parameters of each sigma for core under several ionic conditions. We will study the competition of these various sigmas for core polymerase in purified in vitro systems. We will use our binding results to model the multiple interactions among sigmas and core. We will perturb in vivo conditions by inducing moderate overproduction of a sigma and then determine the effect of this perturbation on the expression of genes under the control of each of the seven sigmas using DNA microarrays. In this way we will test the hypothesis that global regulation of transcription is determined by sigma competition for core. To explore the medical implications of our results. Detailed knowledge of the interactions of sigma-70 and other sigmas with core has potential medical applications. A long-term goal of our studies is to learn enough to devise specific small molecules that will interfere with these key interactions. We will identify peptides and/or small molecules that bind to and interfere with sigma-core binding. This might lead to the development of a new class of **antibiotics.**

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

- **Project Title: SAFE ALTERNATIVE SOLVENTS FOR ANTIBIOTICS EXTRACTION**

  Principal Investigator & Institution: Clark, Jennifer F.; Eltron Research, Inc. 4600 Nautilus Ct S Boulder, Co 803013241

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

  Summary: (provided by applicant): This research will result in identification of non-volatile, non-flammable room temperature ionic liquids (RTIL's) to replace the toxic, flammable, volatile organic compound (VOC) solvents used for extraction of **antibiotics**

from fermentation broths. The solvents used for penicillin extraction include methyl isobutyl ketone, amyl acetate, butyl acetate, and chloroform. These solvents are toxic, irritants, volatile, and extremely flammable. RTIL's have attracted significant attention for green chemistry applications. They are ionic compounds that have very large liquids ranges. Some are air and water stable and immiscible with water. They solubilize aromatics and carbonyls particularly well, so should be effective for **antibiotics** extraction. RTIL's have been studied for liquid-liquid extraction and other separations. Being non-volatile, they are recyclable, and their large liquids ranges allow efficient separations using temperature control. They are non-flammable. They are "tunable" solvents, as the cations can be substituted and/or paired with different anions to manipulate the properties of the liquids and tailor them for specific applications. The use of RTIL's instead of the toxic, flammable, VOC solvents now used would improve the health and safety of pharmaceutical workers, and reduce costs, since they are straightforward to synthesize, and are recyclable. New processes or equipment would not be required. PROPOSED COMMERCIAL APPLICATION: NOT AVAILABLE

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- **Project Title: SOLID-STATE NMR STUDIES OF ANTIMICROBIAL PEPTIDES**

  Principal Investigator & Institution: Hong, Mei; Assistant Professor; Chemistry; Iowa State University of Science & Tech Ames, Ia 500112207

  Timing: Fiscal Year 2003; Project Start 01-FEB-2003; Project End 31-JAN-2008

  Summary: (provided by applicant): Antimicrobial peptides are evolutionarily highly preserved elements of the innate immune system in animals. They kill a wide range of microbial organisms such as bacteria, viruses, and fungi with high potency and speed. Their remarkable ability to prevent pathogenic resistance makes these peptides a viable alternative to conventional **antibiotics.** The broad objective of this research is to elucidate the structural basis for antimicrobial action, so that new and improved **antibiotics** with strong microbiocidal activity but low cytotoxicity to mammalian cells may be designed. The central hypothesis of this project is that antimicrobial peptides share common mechanisms of action that derive from the special characteristics of microbial membranes such as radius of curvature, surface charge, and lack of cholesterol, characteristics that are distinct from mammalian membranes. To test this hypothesis, we will specifically determine the interactions of two representative peptides with lipid bilayers that mimic bacterial, retroviral, and human erythrocyte membranes; determine the orientation topology of these peptides in these various lipid membranes; and measure the secondary structure and aggregation state of these peptides. The peptides of choice are protegrin-1 (PG-1) and rhesus theta-defensin 1 (RTD-1), which both possess a disulfide-bond stabilized beta-sheet conformation that is common to a large number of antimicrobial peptides, including the defensins found in humans. We will use an integrated solid-state nuclear magnetic resonance (NMR) approach to study the mechanism of action of these two beta-sheet peptides. The important lipid factors in antimicrobial selectivity will be identified by studying the lipid-peptide interactions in lipids with defined membrane curvature, cholesterol content, and anionic surface charges. 31P and 2H NMR will be used as the main probes for the lipid-peptide interaction. Information on the peptide orientation in the lipid bilayer is important for understanding whether the peptides disrupt the cell membrane by pore formation or by micellization. This information will be obtained by 13C and 15N NMR experiments using both oriented and unoriented static samples. The ability to extract molecular orientation using unoriented samples will allow us to measure the concentration-dependence and membrane-curvature-dependence of the peptide

orientation. The secondary structure and aggregation of PG-1 and RTD-1 in lipid bilayers will be determined from NMR isotropic chemical shifts and multiple-quantum experiments, respectively. Together, the new structural information, correlated with the characteristics of lipid membranes, will significantly advance our understanding of the mechanism of action of beta-sheet antimicrobial peptides. Moreover, the proposed research will fill our knowledge gap of how beta-sheet peptides interact with lipid bilayers in general.

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- **Project Title: STRUCTURAL STUDIES ON RIBOSOMES AND ANTIBIOTICS**

  Principal Investigator & Institution: Ramakrishnan, Venkatraman R.; Group Leader; Medical Research Council University Post-Grad Med Sch Cambridge,

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

  Summary: (provided by applicant): The ribosome is the large nucleoprotein complex that uses mRNA as the template and aminoacylated tRNAs as substrates to catalyze protein synthesis in all cells. Ribosomes consist of two subunits in all organisms, designated 30S and 50S in bacteria, which together form the 70S ribosome. The 30S subunit improves the fidelity of translation by monitoring codon-anticodon interactions, while the 50S catalyzes peptide bond formation. Both subunits act in concert during translocation, which involves the movement of mRNA and tRNA through the ribosome. Many clinically important **antibiotics** target the bacterial ribosome. Recent advances, including those from our own laboratory, have resulted in high resolution structures of each subunit and a medium resolution structure of the whole 70S ribosome. These structures have revolutionized our understanding of ribosome structure and function. This is a proposal to build on these advances. We have elucidated the interactions of several **antibiotics** with the 30S subunit, and propose to determine the structure of several important remaining ones. We shall also determine the structure of the 30S subunit in complex with initiation factors, protein S1, and with a variety of tRNA and mRNA combinations that involve non-standard pairing or modified bases at the third position of the codon, the wobble position. A special RNA called tmRNA, because it has both tRNA and mRNA-like properties, is used by the cell to rescue ribosomes stalled on defective messages. We shall determine the structure of the ribosome in complex with tmRNA in various states. We shall also crystallize complexes of the ribosome specifically arrested at various points along the translation pathway. Solution of crystal structures of these complexes will shed light on the mechanisms involved during translation, including the interaction of factors with the ribosome and conformational changes during translation. These studies will not only shed light on fundamental aspects of translation, a central process in all cells, but also reveal how many **antibiotics** interact with the ribosome. Such knowledge could help improve existing **antibiotics** and could also lead to the design of new ones.

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

- **Project Title: STRUCTURE AND DYNAMICS OF RIBOSOME FUNCTIONAL SITES**

  Principal Investigator & Institution: Zimmermann, Robert A.; Professor; Biochem and Molecular Biology; University of Massachusetts Amherst 408 Goodell Building Amherst, Ma 01003

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

  Summary: (provided by applicant): The long-term goal of the proposed research is to obtain a detailed description of ligand-ribosome interactions during peptide bond

formation, based on the hypothesis that the ribosome is a dynamic entity whose moving parts promote translation. Although recent high-resolution cryo-EM and crystallographic images provide new insights into the mechanism of translation, these 'snapshots' do not explain how the ribosome interacts with its numerous ligands or how structural changes in the ribosome facilitate this process. The specific objectives of this proposal are to define the structural and functional relationships between tRNA and the components of the peptidyl transferase center (PTC) and the exit site (E site) of the E. coil 50S ribosomal subunit, using chemical, biochemical and genetic approaches. (1) Putative differences in the structural organization of the PTC of archaeal and (eu)bacterial ribosomes, as well as possible changes in the position of tRNA relative to 23S rRNA during peptidyl transfer, will be examined by qualitative and quantitative analysis of the pattern of short-range, photochemically-induced crosslinks to the PTC from the 3' nucleotide of tRNA at the P and A sites and a transition-state analog that spans both. (2) Crystallography and tRNA crosslinking have revealed that there is a protein, L27, at or near the PTC of the (eu)bacterial 50S ribosomal subunit, a region that is otherwise composed entirely of RNA. Moreover, deletion of L27 leads to severe defects in translation. The functional role of L27 will be assessed by investigating the effects of specific truncations on cell growth and ribosome activity, and the site of tRNA crosslinking in L27 will be determined. (3) Protein L1 and its associated RNA comprise a flexible and semi-autonomous domain within the 50S subunit that appears to promote the release of deacyated tRNA from the ribosome following peptide bond formation. To test this theory, the ability of tRNA to interact with L1- RNA fragement complexes will be checked in vitro and the the effects of specific mutations in L1 and the 23S rRNA on tRNA release will be investigated in vivo. (4) As the main contribution of 23S rRNA to the catalysis of peptide bond formation may be to correctly position the peptidyl- and amnioacyl-tRNA substrates, mutations in the 23S rRNA at the PTC may disrupt this process. This hypothesis will be tested by evaluating the pattern of crosslinks between the 3' ends of P- and A-site tRNA and ribosomes containing mutant 23S rRNA. As many **antibiotics** target the ribosome, a detailed understanding of protein synthesis will contribute to the rational development of new **antibiotics** which are urgently needed in the face of widespread **antibiotic** resistance among pathogenic microorganisms.

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- **Project Title: STRUCTURE-BASED ANTIMICROBIAL DESIGN**

  Principal Investigator & Institution: Axelsen, Paul H.; Associate Professor; Pharmacology; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

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

  Summary: (adapted from applicant's abstract): This is a proposal to apply the techniques of X-ray crystallography, molecular dynamics simulation, and infrared spectroscopy, with organic synthesis, in a coordinated interdisciplinary effort to better understand ligand recognition by glycopeptide **antibiotics,** and develop new agents effective against vancomycin-resistant bacteria. We aim to determine the structure of ligand complexes with glycopeptide **antibiotics** using X-ray crystallography, experimentally verify aspects of ligand recognition behavior predicted by computer simulation, and synthetically alter the natural specificity of glycopeptide **antibiotic** in a way which enhances its affinity for cell wall fragments of vancomycin-resistant bacteria. We emphasize the use of molecular dynamics computer simulations for interpreting results and guiding experimental strategies. The overall aim is to confront the emerging health threat of vancomycin-resistance by facilitating the rational design of drugs, and gain insight into the physico-chemical basis of specific molecular recognition.

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- **Project Title: SYNTHESIS & BIOLOGICAL /BIOCIDAL EVALUATION OF ORGANOTIN**

  Principal Investigator & Institution: Pannell, Keith H.; Professor; University of Texas El Paso El Paso, Tx 79968

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

  Summary: (provided by applicant): We propose a continuation of our initially successful study concerning the synthesis and biocidal evaluation of new organotin materials and compounds. Our initial hypothesis that mixed, "heteroleptic" organotins could exhibit a greater activity than that predicted by a simple linear variation of substituent has proven correct. Thus the mixed aryl/alkyl organotin Aryl2AIkylSnCl, arylAlkyl2SnCl, ArylAlkylSnCl2 containing various substituents will continue to be a partial focus of this research. The incorporation of sulfur, oxygen and selenium atoms within the molecular structure also offers a great opportunity for new materials and activities and will be investigated. A new series of di-tin compounds are proposed, ClR2Sn-R'-R2SnCl, R'=aryl, alkyl, where the presence of two active tin sites within the molecular structure present a special and exciting new opportunity for biological activity. We also propose a study of the organotins for the formation of **antibiotic** surfaces. We have preliminary evidence that mixtures of structurally dissimilar organotin chlorides create new solid state phases, hence cooperativity in this area could be important. A series of ionophore-organotins will be synthesized - they are unknown materials with a great capacity for unique biocidal activity. Together with the synthesis of the new materials, complete chemical characterization, including NMR and single crystal structural evaluation is proposed. In El Paso, we shall use an iterative process for continuous biocidal evaluation using a well-understood suite of bacteria, including the very sensitive luminescent marine bacteria that provide a rapid initial evaluation. A second investigation into the potential cooperativity of activity involves the combination of known **antibiotics,** e.g. nalidixic acid and organotins. There are literature hints that such cooperativity may be important. Certainly the capacity of such Lewis base **antibiotics** to form direct interactions with the Lewis acid organotins is clear, thus this is a promising new area of study. Since our initial biocidal screening is performed with a simple suite of bacteria we have enlarged this aspect of our study by collaborating with two research teams outside of the U.T. El Paso campus, namely Dr. Margaret Whalen, Tennessee State University, and Dr. George Eng, University of the District of Columbia. Both are specialists in various forms of biocidal activity evaluation (detailed within the proposal) in areas far from the capacity of the PI, but forming an integral portion of the iterative research activity described. Letters of agreement are attached.

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

- **Project Title: SYNTHESIS OF BLEOMYCIN GROUP ANTIBIOTICS AND ANALOGUES**

  Principal Investigator & Institution: Hecht, Sidney Michael.; President; Chemistry; University of Virginia Charlottesville Box 400195 Charlottesville, Va 22904

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

  Summary: (Principal Investigator's) The long term goals of this research are i) synthesis of bleomycin group **antibiotics** and the development of new methods that facilitate their elaboration, and ii) synthesis of bleomycin analogues that have superior properties as therapeutic agents or which can be used to help define the mechanism of action of

bleomycin. For the period of requested support, the specific aims include completion of the total synthesis of phleomycin and a stereocontrolled, total synthesis of tallysomycin. Also planned are the syntheses of bleomycin analogues that can help to define the mode of DNA binding, which bind and cleave RNA with greater affinity, and which exhibit greater efficiency in double-strand cleavage of B-form DNA. While bleomycin is an established member of the armamentarium of clinically used antitumor agents, there are nonetheless a number of deficiencies in the understanding of the way in which BLM functions as an antitumor agent. The studies proposed here should facilitate an understanding of the mechanism of BLM action and make it possible to identify BLM congeners exhibiting enhanced properties as antitumor agents.

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

- **Project Title: SYNTHETIC/MECHANISTIC STUDIES OF BIOACTIVE MARINE AGENTS**

  Principal Investigator & Institution: Romo, Daniel; Associate Professor; Chemistry; Texas A&M University System College Station, Tx 778433578

  Timing: Fiscal Year 2001; Project Start 01-AUG-1995; Project End 31-JUL-2004

  Summary: (Principal Investigator's Abstract) The objectives of the proposal include total synthesis and biomechanistic studies of the marine natural products pateamine A, palau'amine, gymnodimine, and phakellin which possess novel structures and exhibit potent physiological effects. Natural products that have strong and specific cellular effects have proven to be powerful biochemical probes for dissecting molecular mechanisms of signal transduction pathways involved in various cellular functions. Pateamine A and palau'amine are potent immunosuppressive agents that promise to be useful biochemical probes for elucidating cellular events involved in the immune response. Thus, these natural products may potentially lead to new therapeutic targets for not only organ transplantation therapy, but also diabetes, multiple sclerosis, and rheumatoid arthritis. Gymnodimine is a potent marine toxin that possesses an unusual spirocyclic imine moiety. Its precise molecular mechanism of toxicity has not been elucidated although it appears to be unique. Marine toxins have proven useful for the study of ion channels, protein phosphatases, and neurotransmitter receptors. Thus, gymnodimine promises to be a useful biochemical probe for studies of neuronal function. Phakellin has been proposed to be responsible for the powerful **antibiotic** effects observed in extracts from the marine sponge Phakellia flabellata. Considering the rise in **antibiotic** resistance in recent years, the search for novel **antibiotics** has intensified. The utility of the tetracylic guanidine structure in phakellin and congeners as new **antibiotics** will be assayed. A naturally conjoined objective in our total synthesis efforts is the development of new synthetic methods and strategies for the concise synthesis of these targets. In this regard, several new methods and strategies including formylation of vinyl halides, Hantzsch thiazole synthesis with unactivated bromoketones, Diel-Alder reactions of alpha-exomethylene lactams and vinyl imidazolidinones, a single pot lactam to cyclic imine synthesis, an intramolecular chlorination/1,2 shift sequence, and the use of latent pyrroles will be studied. The synthetic products resulting from this research will enable us and our collaborators Prof. Jun Liu (MIT) and Dr. Chris Miles (AgResearch) to address questions of biological and thus health significance.

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

- **Project Title: THE MOLECULAR CONTROL OF BACTERIAL AUTOLYSIS**

  Principal Investigator & Institution: Bayles, Kenneth W.; Associate Professor; Microbiol/Molec Biol & Biotech; University of Idaho Moscow, Id 838443020

  Timing: Fiscal Year 2003; Project Start 01-JUL-1997; Project End 31-DEC-2007

  Summary: (provided by applicant): Studies of the Staphylococcus aureus lytSR regulatory locus have led to the identification of a complex regulatory system that controls the activity of peptidoglycan hydrolases produced by the cell. One component of this regulation is the IrgAB operon whose expression has been shown to inhibit murein hydrolase activity and cause tolerance to penicillin. It has been proposed that the products of this operon function in a manner analogous to bacteriophage-encoded antiholins, which are membrane-associated proteins that inhibit peptidoglycan hydrolase activity at the postranslational level. Recently, homologous proteins encoded by the S. aureus cid operon have been identified and studied. Preliminary experiments indicate that this operon encodes the holin component of this system that enhances peptidoglycan hydrolase activity and increases sensitivity to penicillin. The possibility that the Irg and cid operons are involved in a bacterial programmed cell death (PCD) mechanism has been indicated since the cid mutant exhibits tolerance to other bactericidal agents besides penicillin. These include rifampicin and mitomycin C, which have distinct cellular targets suggesting that this system responds to nonspecific cellular stress by inducing cell death. The recent finding that cid expression is dependent on the alternate stress response sigma factor, Sigma B, strengthens this hypothesis. The experiments described in this proposal are based on four specific aims. The first aim utilizes a genetic approach to explore the role the cid and Irg gene products during the bactericidal response to **antibiotics** and biocides. The second aim includes flow cytometric studies of membrane potential and cell wall pH designed to more clearly define the roles of the cid and Irg gene products in the regulation of murein hydrolase activity. Purification and analysis of the cid and Irg gene products is the third aim of this proposal with the goal of defining the interactions of these proteins prior to and during cell death. Finally, the fourth aim will study the regulation of cid transcription using molecular strategies to examine the kinetics of cid expression, the cis-acting elements necessary for normal regulation, and the role of a putative transcription activator protein. The long-term objectives of this study are to establish the roles that the Irg and cid operons play in the molecular control of bacterial PCD and to explore novel new therapeutic strategies to combat bacterial infection.

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

- **Project Title: TRANSCRIPTIONAL REGULATION OF OXIDATIVE DEATH**

  Principal Investigator & Institution: Ratan, Rajiv R.; Director; Massachusetts General Hospital 55 Fruit St Boston, Ma 02114

  Timing: Fiscal Year 2003; Project Start 15-APR-2003; Project End 31-MAR-2008

  Summary: Huntington's Disease (HD) is an autosomal dominant disorder resulting from selective loss of neurons in the striatum and cerebral cortex. Loss of neurons in HD results from pathological expansion of CAG repeats encoding glutamine. Though the precise mechanisms by which glutamine repeats lead to neuronal loss in HD are unclear, oxidative stress, apoptosis, and transcriptional dysregulation have all been implicated in disease pathogenesis. To understand better oxidative and transcriptional mechanisms that may lead to neuronal loss in HD, we have utilized an in vitro model of oxidative stress in primary cortical neurons. In preliminary studies we have shown that oxidative cell death can be fully abrogated by sequence-selective DNA binding drugs,

including mithramycin A (MMA) and chromomcyin A3. These agents are members of the aureolic acid antitumor **antibiotics** that share a common chromophore, aglycon ring, but differ in the nature of the sugar moieties connected to either side of the aglycone ring. Both **antibiotics** inhibit transcription during macromoleclar biosynthesis by binding to the "GC" rich transcriptional response elements. To test whether aureolic **antibiotics** can protect neurons in an in vivo model ofneurodegeneration that may inolve oxidative stress, we examined the effect of MMA in the R6/2 transgenic model of HD. We found that MMA prolongs survival in these mice by nearly 30%, a magnitude superior to any other single neuroprotective agent. These preliminary data are consistent with the overall hypothesis to be tested in this proposal: MMA inhibits neuronal death due to oxidative stress and/or mutant Huntington protein in vitro and in vivo by inhibiting the binding of pro-apoptotic zinc finger transcription factors such as TIEG, and enhancing the DNA binding of pro-survival transcription factors such as CREB. We will examine this hypothesis by determining whether protective concentrations of MMA inhibit TIEG binding to its GC rich DNA binding sites and whether TIEG is critical for oxidative death in cortical neurons. In the second aim, we will determine how MMA affects CREB DNA binding and whether increases in CREB DNA binding contribute to MMA's salutary effects. In the last specific aim, we will compare the mechanism of neuroprotection of MMA to those ofhistone deacetylase inhibitors, another class of transcriptional regulators. These studies will provide critical, mechanistic data on neuroprotective modulators of transcription.

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

- **Project Title: TRANSLATIONAL CONTROL MEDIATED BY MRNA STRUCTURE**

  Principal Investigator & Institution: Kozak, Marilyn S.; Professor; Biochemistry; Univ of Med/Dent Nj-R W Johnson Med Sch Robert Wood Johnson Medical Sch Piscataway, Nj 08854

  Timing: Fiscal Year 2001; Project Start 01-MAR-1990; Project End 31-JUL-2003

  Summary: This project concerns the mechanism by which eukaryotic ribosomes engage messenger RNA and select the AUG start codon. The scanning model for initiation of translation postulates that the 40S ribosomal subunit enters at the 5' end of the mRNA and advances linearly to the first AUG condon. In vertebrate mRNAs, a sequence flanking the AUG condon (GCCACCaugG) augments the stop-scanning step. In Specific Aim 1 aspects of the scanning mechanism will be investigated by using a primer-extension inhibition (toeprinting) assay that was recently adapted for eukaryotic translation systems. The processivity of scanning will be assessed by monitoring the movement of 40S ribosomal subunits over long distances, with and without secondary structure, under a variety of conditions. A two-stage assay will be developed to enable scanning to be studied separately from the ribosome-entry step. **Antibiotics** will be screened to identify agents that might target a specific type of leader sequence. Other projects will test for a saturable component that might recognize the GCCACC motif and for alternative sequences that might function in rare mRNAs that lack the consensus sequence. Specific Aim 2 will investigate aspects of the reinitiation mechanism. Ribosomes that accumulate at a point of blockage (a pseudoknot in the upstream ORF) will be analyzed to identify factors, required for reinitiation, that dissociate when the elongation phase of translation is prolonged. Other experiments will determine whether the structure that scans in the reinitiation mode is a 40S or a "loosened" 80S ribosome. In Specific Aim 3 chemical footprinting techniques will be used for the first time to probe eukaryotic ribosome/mRNA complexes. Substrates will include conventional 48S and 80S initiation complexes as well as novel complexes in which scanning 40S subunits are

caught in midstream. Effects of **antibiotics** on interactions with the AUG codon and GCCACC motif will be studied. Footprints will be monitored for ATP-mediated changes that might indicate opening and closing of a clamp. The reason why 40S ribosome/factor complexes protect "extra" sequences, which are accessible to RNase in 80S initiation complexes, will be studied.

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

- **Project Title: TREATMENT OF PERIODONTAL INFECTIONS**

  Principal Investigator & Institution: Goodson, J Max.; Forsyth Institute Boston, Ma 02115

  Timing: Fiscal Year 2001; Project Start 01-JUN-1999; Project End 31-MAY-2004

  Summary: This project seeks to evaluate the most promising means to eradicate infections caused by 0eriodontal disease pathogens. Considering that scaling and root planing (SRP) is likely to be essential to rid sites of plaque biofilms and infected calculus, four adjunctive strategies appear likely to substantially contribute to the transmission, disinfection of pathogen reservoirs and elimination of environments that support growth of periodontal pathogens. Based on a review of microbiologic responses described in our previous studies and in the literature, the strategies most likely to eliminate or suppress the periodontal pathogens were identified. Reduction of supragingival plaque will be achieved by providing powered toothbrushes and triclosan/co-polymer dentifrice to all subjects. Control of pathogen transmission will be by chlorhexidine (CHX) mouth-rinses for two weeks following completion of therapy. Disinfection of pathogen reservoirs will be by application of tetracycline (TC) fibers in all pockets > 3mm. Elimination of environments that support growth of periodontal pathogens will be by periodontal surgery. The proposal describes a unique 2/3 factorial design in which local **antibiotics,** systemic **antibiotics** and periodontal surgery will be compared as adjunctive treatments following SRP in subjects receiving electric toothbrushes and triclosan-co-polymer dentifrice. The experimental design provides the potential for high statistical sensitivity by evaluating main effects through combined analysis of 4 of the 8 experimental groups. In addition, the model provides a means to evaluate important interactions between each of the treatments being tested. Although this study addresses important questions related to clinical practice, it also provides information on biological effects of various forms of therapy and identifies the most important directions to be taken in future investigations.

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

- **Project Title: X-RAY STUDIES OF SUGAR-MODIFYING ENZYMES**

  Principal Investigator & Institution: Holden, Hazel M.; Professor; Institute for Enzyme Research; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2002; Project Start 01-JUN-1994; Project End 31-MAY-2006

  Summary: Nucleotide-linked sugars are found in all organisms where they fulfill a variety of important biological roles. In galactose metabolism, which has been one of the main focuses of this laboratory for twelve years, the sugar is attached to UDP. Interestingly, many of the deoxysugars, which display wide ranges of biological activities from mediating cell-cell interactions to serving as components in various **antibiotics,** are synthesized via biochemical pathways starting with the attachment of alpha-D-glucose-1 phosphate to either CDP or TDP. The overall goal of this grant renewal is to understand by x-ray crystallographic and site-directed mutagenesis techniques, the structures of enzymes that specific modify nucleotide-linked sugars. The systems that will be investigated include human UDP-galactose 4-epimerase, CDP-D-

tyvelose 2-epimerase from Y. pseudotuberculosis IVA, 2,3-d4ehydratase from S. fradiae, and seven enzymes isolated from S. venezuelae that are involved in the biosynthesis of desosamine. UDP-galactose 4-epimerase functions in galactose metabolism by catalyzing the interconversion of UDP-galactose and UDP-glucose. CDP-tyvelose. Tyvelose occurs in the O-antigens of some types of gram-negative bacteria. These 2,3-dehydratase to be studied catalyzes the first step in mycarose biosynthesis. Both mycarose and desosamine are deoxysugars found in some macrolide **antibiotics** such as erythromycin. The research on UDP-galactose 4-epimerase is in its final stage. The proposed studies on enzymes involved deoxysugars biosynthesis are completely new. Ultimately new structural analysis will yield detailed three-dimensional descriptions of protein: ligand interactions and may eventually provide a molecular foundation upon which to base the design of new antimicrobial agents.

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

- **Activities of the Combination of Quinupristin-Dalfopristin with Rifampin In Vitro and in Experimental Endocarditis Due to Staphylococcus aureus Strains with Various Phenotypes of Resistance to Macrolide-Lincosamide-Streptogramin Antibiotics.** by Zarrouk V, Bozdogan B, Leclercq R, Garry L, Feger C, Carbon C, Fantin B.; 2001 Apr; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=90450
- **Amino Acid Sequence Requirements at Residues 69 and 238 for the SME-1 [beta]-Lactamase To Confer Resistance to [beta]-Lactam Antibiotics.** by Majiduddin FK, Palzkill T.; 2003 Mar; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=149323
- **Antibiotic Activity and Characterization of BB-3497, a Novel Peptide Deformylase Inhibitor.** by Clements JM, Beckett RP, Brown A, Catlin G, Lobell M, Palan S, Thomas W, Whittaker M, Wood S, Salama S, Baker PJ, Rodgers HF, Barynin V, Rice DW, Hunter MG.; 2001 Feb; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=90327

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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.

- **Antibiotic activity in microbiological media versus that in human urine: comparison of ampicillin, ciprofloxacin, and trimethoprim-sulfamethoxazole.** by Drobot GR, Karlowsky JA, Hoban DJ, Zhanel GG.; 1996 Jan; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=163091
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- **Antibiotic Treatment of Experimental Pneumonic Plague in Mice.** by Byrne WR, Welkos SL, Pitt ML, Davis KJ, Brueckner RP, Ezzell JW, Nelson GO, Vaccaro JR, Battersby LC, Friedlander AM.; 1998 Mar; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=105516
- **Antibiotic-impregnated cement and beads for orthopedic infections.** by Wininger DA, Fass RJ.; 1996 Dec; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=163602
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- **Can penicillins and other beta-lactam antibiotics be used to treat tuberculosis?** by Chambers HF, Moreau D, Yajko D, Miick C, Wagner C, Hackbarth C, Kocagoz S, Rosenberg E, Hadley WK, Nikaido H.; 1995 Dec; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=163000
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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 antibiotics, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "antibiotics" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for antibiotics (hyperlinks lead to article summaries):

- **A case of Leuconostoc ventriculitis with resistance to carbapenem antibiotics.**
  Author(s): Deye G, Lewis J, Patterson J, Jorgensen J.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 2003 September 15; 37(6): 869-70.
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  Author(s): Calfee DP, Brooks J, Zirk NM, Giannetta ET, Scheld WM, Farr BM.
  Source: The Journal of Hospital Infection. 2003 September; 55(1): 26-32.
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- **A simple intervention to improve hospital antibiotic prescribing.**
  Author(s): Damodaran SS.
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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: The Journal of Allergy and Clinical Immunology. 2003 September; 112(3): 629-30.
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  Author(s): Innes HE, Smith DB, O'Reilly SM, Clark PI, Kelly V, Marshall E.
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  Source: The British Journal of General Practice : the Journal of the Royal College of General Practitioners. 2003 June; 53(491): 491-2.
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  Author(s): Hall M.
  Source: Jama : the Journal of the American Medical Association. 2003 October 8; 290(14): 1851; Author Reply 1851.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14532304&dopt=Abstract

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  Author(s): Lin TY.
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  Source: Critical Care (London, England). 2003 October; 7(5): 351-3. Epub 2003 March 17. Review.
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  Author(s): Grantmakers In Health, Washington, D.C., USA.
  Source: Issue Brief (Grantmakers Health). 2000 October 3; (7): 1-26.
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  Author(s): Hoth JJ, Franklin GA, Stassen NA, Girard SM, Rodriguez RJ, Rodriguez JL.
  Source: The Journal of Trauma. 2003 August; 55(2): 249-54.
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  Author(s): van de Wetering MD, van Woensel JB.
  Source: Cochrane Database Syst Rev. 2003; (2): Cd003295. Review.
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  Author(s): Norris P, Toner E, Morris K.
  Source: N Z Med J. 2003 July 11; 116(1177): U505. No Abstract Available.
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  Author(s): Dietera A, Hamm A, Fiedler HP, Goodfellow M, Muller WE, Brun R, Beil W, Bringmann G.
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  Author(s): Spreer A, Kerstan H, Bottcher T, Gerber J, Siemer A, Zysk G, Mitchell TJ, Eiffert H, Nau R.
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  Author(s): Wilton L, Kollarova M, Heeley E, Shakir S.
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  Author(s): Liu SP, Hu XL, Luo HQ.
  Source: Anal Sci. 2003 June; 19(6): 927-32.
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  Author(s): Jaswal RS, Kaushal RK, Goel A, Pathania K.
  Source: Indian Pediatrics. 2003 September; 40(9): 880-3.
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  Author(s): White R.
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  Source: The Journal of Antimicrobial Chemotherapy. 2003 July; 52(1): 5-7. Epub 2003 June 12. Review. Erratum In: J Antimicrob Chemother. 2003 August; 52(2): 317.
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  Source: Med J Malaysia. 2003 June; 58(2): 262-7.
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- **Staphylococcus aureus bacteremia: recurrence and the impact of antibiotic treatment in a prospective multicenter study.**
  Author(s): Chang FY, Peacock JE Jr, Musher DM, Triplett P, MacDonald BB, Mylotte JM, O'Donnell A, Wagener MM, Yu VL.
  Source: Medicine; Analytical Reviews of General Medicine, Neurology, Psychiatry, Dermatology, and Pediatrics. 2003 September; 82(5): 333-9.
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- **Staphylococcus aureus carriage in selected communities and their antibiotic susceptibility patterns.**
  Author(s): Norazah A, Lim VK, Munirah SN, Kamel AG.
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  Author(s): Kerr C.
  Source: The Lancet Infectious Diseases. 2003 September; 3(9): 529.
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  Author(s): Moyo SR, Maeland JA, Munemo ES.
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- **The effect of antibiotics on elevated serum prostate specific antigen in patients with urinary symptoms and negative digital rectal examination: a pilot study.**
  Author(s): Bulbul MA, Wazzan W, Hijaz A, Shaar A.
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- **The inventory of antibiotics in Russian home medicine cabinets.**
  Author(s): Stratchounski LS, Andreeva IV, Ratchina SA, Galkin DV, Petrotchenkova NA, Demin AA, Kuzin VB, Kusnetsova ST, Likhatcheva RY, Nedogoda SV, Ortenberg EA, Belikov AS, Toropova IA.
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- **The role of prophylactic antibiotics in plastic surgery: whom are we treating?**
  Author(s): Rohrich RJ, Rios JL.
  Source: Plastic and Reconstructive Surgery. 2003 August; 112(2): 617-8.
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  Source: Hepatogastroenterology. 2003 July-August; 50(52): 1133-5.
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- **Use of antibiotics in upper respiratory infections on patients under 16 years old in private ambulatory medicine.**
  Author(s): Pelaez-Ballestas I, Hernandez-Garduno A, Arredondo-Garcia JL, Viramontes-Madrid JL, Aguilar-Chiu A.
  Source: Salud P'ublica De M'exico. 2003 May-June; 45(3): 159-64.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12870416&dopt=Abstract

- **Variation in use of broad-spectrum antibiotics for acute respiratory tract infection.**
  Author(s): Mainous AG 3rd, Hueston WJ.
  Source: Jama : the Journal of the American Medical Association. 2003 June 4; 289(21): 2797; Author Reply 2797-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12783910&dopt=Abstract

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  Author(s): Karnath BM, Luh JY.
  Source: Jama : the Journal of the American Medical Association. 2003 June 4; 289(21): 2796-7; Author Reply 2797-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12783909&dopt=Abstract

- **Which members of a community need antibiotics to control trachoma? Conjunctival Chlamydia trachomatis infection load in Gambian villages.**
  Author(s): Burton MJ, Holland MJ, Faal N, Aryee EA, Alexander ND, Bah M, Faal H, West SK, Foster A, Johnson GJ, Mabey DC, Bailey RL.
  Source: Investigative Ophthalmology & Visual Science. 2003 October; 44(10): 4215-22.
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# CHAPTER 2. NUTRITION AND ANTIBIOTICS

## Overview

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

## Finding Nutrition Studies on Antibiotics

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 "antibiotics" (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 antibiotics:

- **Acid-accelerated DNA-cleaving activities of antitumor antibiotic varacin.**
  Author(s): Open Laboratory of Chirotechnology, Institute of Molecular Technology for Drug Discovery and Synthesis, Department of Applied Biology and Chemical Technology, Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong.
  Source: Lee, A H Chan, A S Li, T Chem-Commun-(Camb). 2002 September 21; (18): 2112-3 1359-7345
- **Alternatives to antibiotic use: probiotics for the gut.**
  Author(s): Canadian Research and Development Centre for Probiotics, Lawson Health Research Institute, London, Ontario. gregor@uwo.ca
  Source: Reid, G Friendship, R Anim-Biotechnol. 2002 May; 13(1): 97-112 1049-5398
- **Alternatives to the use of antibiotics as growth promoters for monogastric animals.**
  Author(s): Wageningen University, Dept. of Animal Sciences, The Netherlands.
  Source: Verstegen, M W Williams, B A Anim-Biotechnol. 2002 May; 13(1): 113-27 1049-5398
- **Antibiotics as growth promotants: mode of action.**
  Author(s): University of Illinois at Urbana-Champaign, 61801, USA.
  Source: Gaskins, H R Collier, C T Anderson, D B Anim-Biotechnol. 2002 May; 13(1): 29-42 1049-5398
- **Bacteremic and leukopenic pneumococcal pneumonia: successful treatment with antibiotics, pulse steroid, and continuous hemodiafiltration.**
  Author(s): First Department of Internal Medicine, Kurume University School of Medicine, Fukuoka, Japan. yokoyama-t@nyc.odn.ne.jp
  Source: Yokoyama, T Sakamoto, T Shida, N Shimada, T Kaku, N Aizawa, H Oizumi, K J-Infect-Chemother. 2002 September; 8(3): 247-51 1341-321X
- **Carbon flux distribution in antibiotic-producing chemostat cultures of Streptomyces lividans.**
  Author(s): Swammerdam Institute of Life Sciences, University of Amsterdam, Nieuwe Achtergracht 166, Amsterdam, 1018WV, The Netherlands. c.avignone-rossa@surrey.ac.uk
  Source: Avignone Rossa, C White, J Kuiper, A Postma, P W Bibb, M Teixeira de Mattos, M J Metab-Eng. 2002 April; 4(2): 138-50 1096-7176
- **Composition and antibiotic resistance profile of microcosm dental plaques before and after exposure to tetracycline.**
  Author(s): Department of Microbiology, Eastman Dental Hospital, University College London Hospitals NHS Trust, UK. dready@eastman.ucl.ac.uk
  Source: Ready, D Roberts, A P Pratten, J Spratt, D A Wilson, M Mullany, P J-Antimicrob-Chemother. 2002 May; 49(5): 769-75 0305-7453
- **Effect of outer-membrane permeabilizers on the activity of antibiotics and plant extracts against Pseudomonas aeruginosa.**
  Author(s): Biochemistry Division, Regional Research Laboratory, Jorhat 785 006, Assam, India.
  Source: Guha, A Choudhury, A Unni, B G Roy, M K Folia-Microbiol-(Praha). 2002; 47(4): 379-84 0015-5632

- **Enantioselective total synthesis of angucyclinone-type antibiotics rubiginones A(2) and C(2).**
  Author(s): Departamento de Quimica Organica (C-I), Universidad Autonoma Cantoblanco, 28049 Madrid, Spain. carmen.carreno@uam.es
  Source: Carreno, M C Ribagorda, M Somoza, A Urbano, A Angew-Chem-Int-Ed-Engl. 2002 August 2; 41(15): 2755-7 0570-0833

- **Experience of feeding pigs without antibiotics: a European perspective.**
  Author(s): South Dakota State University, Department of Animal Sciences, Brookings 57007, USA.
  Source: Stein, H H Anim-Biotechnol. 2002 May; 13(1): 85-95 1049-5398

- **Oxygen consumption and electron spin resonance studies of free radical production by alveolar cells exposed to anoxia: inhibiting effects of the antibiotic ceftazidime.**
  Author(s): Centre for Oxygen Research and Development, Institut de Chimie, B6a, Domaine Universitaire du Sart Tilman, 4000 Liege, Belgium. amouithys@ulg.ac.be
  Source: Mouithys Mickalad, A Mathy Hartert, M Du, G Sluse, F Deby, C Lamy, M Deby Dupont, G Redox-Repage 2002; 7(2): 85-94 1351-0002

- **Phosphate availability regulates biosynthesis of two antibiotics, prodigiosin and carbapenem, in Serratia via both quorum-sensing-dependent and -independent pathways.**
  Author(s): Department of Biochemistry, University of Cambridge, Cambridge, CB2 1QW, UK.
  Source: Slater, H Crow, M Everson, L Salmond, G P Mol-Microbiol. 2003 January; 47(2): 303-20 0950-382X

- **Prevalence and antibiotic resistance profile of mercury-resistant oral bacteria from children with and without mercury amalgam fillings.**
  Author(s): Department of Microbiology, Eastman Dental Institute, University College London, 256 Gray's Inn Road, London WC1X 8LD, UK.
  Source: Pike, R Lucas, V Stapleton, P Gilthorpe, M S Roberts, G Rowbury, R Richards, H Mullany, P Wilson, M J-Antimicrob-Chemother. 2002 May; 49(5): 777-83 0305-7453

- **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

- **Prospective study of depressive symptoms and quality of life in acne vulgaris patients treated with isotretinoin compared to antibiotic and topical therapy.**
  Author(s): Department of Psychiatry, The University of Melbourne, The Melbourne Clinic, Melbourne, Victoria, Australia. cng@unimelb.edu.au
  Source: Ng, C H Tam, M M Celi, E Tate, B Schweitzer, I Australas-J-Dermatol. 2002 November; 43(4): 262-8 0004-8380

- **The impact of primary antibiotic resistance on the efficacy of ranitidine bismuth citrate- vs. omeprazole-based one-week triple therapies in H. pylori eradication--a randomised controlled trial.**
  Author(s): Department of Hepatogastroenterology, Internal Medicine, General Hospital Sveti Duh, Zagreb, Croatia.
  Source: Bago, J Halle, Z B Strinic, D Kucisec, N Jandric, D Bevanda, M Tomic, M Bilic, A Wien-Klin-Wochenschr. 2002 June 28; 114(12): 448-53 0043-5325

- **Treatment of post-burns bacterial infections by bacteriophages, specifically ubiquitous Pseudomonas spp. notoriously resistant to antibiotics.**
  Author(s): Department of Life Sciences, Nottingham Trent University, Nottingham, England. Shamim.ahmad@ntu.ac.uk
  Source: Ahmad, S I Med-Hypotheses. 2002 April; 58(4): 327-31 0306-9877
- **UCS1025A and B, new antitumor antibiotics from the fungus Acremonium species.**
  Author(s): Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., 3-6-6 Asahimachi, Machida, Japan. tsutomu.agatsuma@kyowa.co.jp
  Source: Agatsuma, T Akama, T Nara, S Matsumiya, S Nakai, R Ogawa, H Otaki, S Ikeda, S Saitoh, Y Kanda, Y Org-Lett. 2002 December 12; 4(25): 4387-90 1523-7060

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

- **Acid-accelerated DNA-cleaving activities of antitumor antibiotic varacin.**
  Author(s): Open Laboratory of Chirotechnology, Institute of Molecular Technology for Drug Discovery and Synthesis, Department of Applied Biology and Chemical Technology, Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong.
  Source: Lee, A H Chan, A S Li, T Chem-Commun-(Camb). 2002 September 21; (18): 2112-3 1359-7345
- **Alternatives to antibiotic use: probiotics for the gut.**
  Author(s): Canadian Research and Development Centre for Probiotics, Lawson Health Research Institute, London, Ontario. gregor@uwo.ca
  Source: Reid, G Friendship, R Anim-Biotechnol. 2002 May; 13(1): 97-112 1049-5398
- **Alternatives to the use of antibiotics as growth promoters for monogastric animals.**
  Author(s): Wageningen University, Dept. of Animal Sciences, The Netherlands.
  Source: Verstegen, M W Williams, B A Anim-Biotechnol. 2002 May; 13(1): 113-27 1049-5398
- **Antibiotics as growth promotants: mode of action.**
  Author(s): University of Illinois at Urbana-Champaign, 61801, USA.
  Source: Gaskins, H R Collier, C T Anderson, D B Anim-Biotechnol. 2002 May; 13(1): 29-42 1049-5398
- **Bacteremic and leukopenic pneumococcal pneumonia: successful treatment with antibiotics, pulse steroid, and continuous hemodiafiltration.**
  Author(s): First Department of Internal Medicine, Kurume University School of Medicine, Fukuoka, Japan. yokoyama-t@nyc.odn.ne.jp
  Source: Yokoyama, T Sakamoto, T Shida, N Shimada, T Kaku, N Aizawa, H Oizumi, K J-Infect-Chemother. 2002 September; 8(3): 247-51 1341-321X
- **Carbon flux distribution in antibiotic-producing chemostat cultures of Streptomyces lividans.**
  Author(s): Swammerdam Institute of Life Sciences, University of Amsterdam, Nieuwe Achtergracht 166, Amsterdam, 1018WV, The Netherlands. c.avignone-rossa@surrey.ac.uk
  Source: Avignone Rossa, C White, J Kuiper, A Postma, P W Bibb, M Teixeira de Mattos, M J Metab-Eng. 2002 April; 4(2): 138-50 1096-7176
- **Composition and antibiotic resistance profile of microcosm dental plaques before and after exposure to tetracycline.**
  Author(s): Department of Microbiology, Eastman Dental Hospital, University College London Hospitals NHS Trust, UK. dready@eastman.ucl.ac.uk

Source: Ready, D Roberts, A P Pratten, J Spratt, D A Wilson, M Mullany, P J-Antimicrob-Chemother. 2002 May; 49(5): 769-75 0305-7453

- **Effect of outer-membrane permeabilizers on the activity of antibiotics and plant extracts against Pseudomonas aeruginosa.**
  Author(s): Biochemistry Division, Regional Research Laboratory, Jorhat 785 006, Assam, India.
  Source: Guha, A Choudhury, A Unni, B G Roy, M K Folia-Microbiol-(Praha). 2002; 47(4): 379-84 0015-5632

- **Enantioselective total synthesis of angucyclinone-type antibiotics rubiginones A(2) and C(2).**
  Author(s): Departamento de Quimica Organica (C-I), Universidad Autonoma Cantoblanco, 28049 Madrid, Spain. carmen.carreno@uam.es
  Source: Carreno, M C Ribagorda, M Somoza, A Urbano, A Angew-Chem-Int-Ed-Engl. 2002 August 2; 41(15): 2755-7 0570-0833

- **Experience of feeding pigs without antibiotics: a European perspective.**
  Author(s): South Dakota State University, Department of Animal Sciences, Brookings 57007, USA.
  Source: Stein, H H Anim-Biotechnol. 2002 May; 13(1): 85-95 1049-5398

- **Oxygen consumption and electron spin resonance studies of free radical production by alveolar cells exposed to anoxia: inhibiting effects of the antibiotic ceftazidime.**
  Author(s): Centre for Oxygen Research and Development, Institut de Chimie, B6a, Domaine Universitaire du Sart Tilman, 4000 Liege, Belgium. amouithys@ulg.ac.be
  Source: Mouithys Mickalad, A Mathy Hartert, M Du, G Sluse, F Deby, C Lamy, M Deby Dupont, G Redox-Repage 2002; 7(2): 85-94 1351-0002

- **Phosphate availability regulates biosynthesis of two antibiotics, prodigiosin and carbapenem, in Serratia via both quorum-sensing-dependent and -independent pathways.**
  Author(s): Department of Biochemistry, University of Cambridge, Cambridge, CB2 1QW, UK.
  Source: Slater, H Crow, M Everson, L Salmond, G P Mol-Microbiol. 2003 January; 47(2): 303-20 0950-382X

- **Prevalence and antibiotic resistance profile of mercury-resistant oral bacteria from children with and without mercury amalgam fillings.**
  Author(s): Department of Microbiology, Eastman Dental Institute, University College London, 256 Gray's Inn Road, London WC1X 8LD, UK.
  Source: Pike, R Lucas, V Stapleton, P Gilthorpe, M S Roberts, G Rowbury, R Richards, H Mullany, P Wilson, M J-Antimicrob-Chemother. 2002 May; 49(5): 777-83 0305-7453

- **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

- **Prospective study of depressive symptoms and quality of life in acne vulgaris patients treated with isotretinoin compared to antibiotic and topical therapy.**
  Author(s): Department of Psychiatry, The University of Melbourne, The Melbourne Clinic, Melbourne, Victoria, Australia. cng@unimelb.edu.au
  Source: Ng, C H Tam, M M Celi, E Tate, B Schweitzer, I Australas-J-Dermatol. 2002 November; 43(4): 262-8 0004-8380

- **The impact of primary antibiotic resistance on the efficacy of ranitidine bismuth citrate- vs. omeprazole-based one-week triple therapies in H. pylori eradication--a randomised controlled trial.**
  Author(s): Department of Hepatogastroenterology, Internal Medicine, General Hospital Sveti Duh, Zagreb, Croatia.
  Source: Bago, J Halle, Z B Strinic, D Kucisec, N Jandric, D Bevanda, M Tomic, M Bilic, A Wien-Klin-Wochenschr. 2002 June 28; 114(12): 448-53 0043-5325
- **Treatment of post-burns bacterial infections by bacteriophages, specifically ubiquitous Pseudomonas spp. notoriously resistant to antibiotics.**
  Author(s): Department of Life Sciences, Nottingham Trent University, Nottingham, England. Shamim.ahmad@ntu.ac.uk
  Source: Ahmad, S I Med-Hypotheses. 2002 April; 58(4): 327-31 0306-9877
- **UCS1025A and B, new antitumor antibiotics from the fungus Acremonium species.**
  Author(s): Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., 3-6-6 Asahimachi, Machida, Japan. tsutomu.agatsuma@kyowa.co.jp
  Source: Agatsuma, T Akama, T Nara, S Matsumiya, S Nakai, R Ogawa, H Otaki, S Ikeda, S Saitoh, Y Kanda, Y Org-Lett. 2002 December 12; 4(25): 4387-90 1523-7060

## 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 antibiotics; 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**
  Alternative names: Vitamin C (Ascorbic Acid)
  Source: Integrative Medicine Communications; www.drkoop.com

  **Folic Acid**
  Alternative names: Vitamin B9 (Folic Acid)
  Source: Integrative Medicine Communications; www.drkoop.com

  **Niacin**
  Alternative names: Vitamin B3 (Niacin)
  Source: Integrative Medicine Communications; www.drkoop.com

  **Riboflavin**
  Alternative names: Vitamin B2 (Riboflavin)
  Source: Integrative Medicine Communications; www.drkoop.com

  **Thiamine**
  Alternative names: Vitamin B1 (Thiamine)
  Source: Integrative Medicine Communications; www.drkoop.com

  **Vitamin B1 (thiamine)**
  Alternative names: Thiamine
  Source: Integrative Medicine Communications; www.drkoop.com

  **Vitamin B12 (cobalamin)**
  Alternative names: Cobalamin
  Source: Integrative Medicine Communications; www.drkoop.com

**Vitamin B2 (riboflavin)**
Alternative names: Riboflavin
Source: Integrative Medicine Communications; www.drkoop.com

**Vitamin B3 (niacin)**
Alternative names: Niacin
Source: Integrative Medicine Communications; www.drkoop.com

**Vitamin B9 (folic Acid)**
Alternative names: Folate
Source: Integrative Medicine Communications; www.drkoop.com

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

**Vitamin K**
Source: Healthnotes, Inc.; www.healthnotes.com

**Vitamin K**
Alternative names: Menadione
Source: Integrative Medicine Communications; www.drkoop.com

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

- **Minerals**

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

**Biotin**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10008,00.html

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

**Calcium**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,884,00.html

**Folate**
Alternative names: Vitamin B9 (Folic Acid)
Source: Integrative Medicine Communications; www.drkoop.com

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

**Iron**
Alternative names: Ferrous Sulfate
Source: Integrative Medicine Communications; www.drkoop.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

**Retinol**
Alternative names: Vitamin A (Retinol)
Source: Integrative Medicine Communications; www.drkoop.com

**Vitamin a (retinol)**
Alternative names: Retinol
Source: Integrative Medicine Communications; www.drkoop.com

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

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

- **Food and Diet**

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

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

**Ferrous Sulfate**
Alternative names: Iron
Source: Integrative Medicine Communications; www.drkoop.com

**Garlic**
Alternative names: Allium sativum
Source: Healthnotes, Inc.; www.healthnotes.com

**Garlic**
Alternative names: Allium sativum
Source: Integrative Medicine Communications; www.drkoop.com

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

**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

**Non-nutritive and Artificial Sweeteners**
Source: Healthnotes, Inc.; www.healthnotes.com

**Vegetarian Diet**
Source: Healthnotes, Inc.; www.healthnotes.com

**Wound Healing**
Source: Healthnotes, Inc.; www.healthnotes.com

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

**Yogurt**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/foods_view/0,1523,97,00.html

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

# CHAPTER 3. ALTERNATIVE MEDICINE AND ANTIBIOTICS

## Overview

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

- **Combining Supplements and Prescription Drugs: What Your Patients Need to Know**

  Source: Alternative and Complementary Therapies. 6(4): 177-183. August 2000.

  Summary: This journal article reviews what patients need to know about combining herbal supplements and prescription drugs. First, it looks at general clinical issues regarding the concomitant use of herbs and drugs. Then, it summarizes the major concerns, including the lack of knowledge about herbs, lack of quality control for herbal supplements, lack of patient communication about the use of botanicals, and lack of practitioner knowledge about potential interactions. Finally, it reviews known interactions between popular herbal supplements and commonly prescribed classes of drugs, including immunostimulant and immunosuppressive drugs, antidepressants, monoamine oxidase inhibitors, **antibiotics,** anticoagulants, antihypertensives and diuretics, hypoglycemics and hyperglycemics, and sedatives. The article includes a list of herb-drug combinations to avoid, a resources list, a summary of advice for patients, a recommended reading list, and 21 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 antibiotics 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 "antibiotics" (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 antibiotics:

- **"Not thrush again!" Women's experience of post-antibiotic vulvovaginitis.**
  Author(s): Pirotta MV, Gunn JM, Chondros P.
  Source: The Medical Journal of Australia. 2003 July 7; 179(1): 43-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12831384&dopt=Abstract

- **A combination effect of epigallocatechin gallate, a major compound of green tea catechins, with antibiotics on Helicobacter pylori growth in vitro.**
  Author(s): Yanagawa Y, Yamamoto Y, Hara Y, Shimamura T.
  Source: Current Microbiology. 2003 September; 47(3): 244-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14570277&dopt=Abstract

- **Additive, indifferent and antagonistic effects in combinations of epigallocatechin gallate with 12 non-beta-lactam antibiotics against methicillin-resistant Staphylococcus aureus.**
  Author(s): Hu ZQ, Zhao WH, Yoda Y, Asano N, Hara Y, Shimamura T.
  Source: The Journal of Antimicrobial Chemotherapy. 2002 December; 50(6): 1051-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12461032&dopt=Abstract

- **Antibiotic associated diarrhoea: a controlled study comparing plain antibiotic with those containing protected lactobacilli.**
  Author(s): Ahuja MC, Khamar B.
  Source: J Indian Med Assoc. 2002 May; 100(5): 334-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12418644&dopt=Abstract

- **Antibiotic resistance among verocytotoxigenic Escherichia coli (VTEC) and non-VTEC isolated from domestic animals and humans.**
  Author(s): Bettelheim KA, Hornitzky MA, Djordjevic SP, Kuzevski A.
  Source: Journal of Medical Microbiology. 2003 February; 52(Pt 2): 155-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12543922&dopt=Abstract

- **Antibiotics and the development of resistant microorganisms. Can homeopathy be an alternative?**
  Author(s): Viksveen P.

Source: Homeopathy. 2003 April; 92(2): 99-107. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12725252&dopt=Abstract

- **Antibiotics for persistent nasal discharge (rhinosinusitis) in children.**
Author(s): Morris P, Leach A.
Source: Cochrane Database Syst Rev. 2002; (4): Cd001094. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12519551&dopt=Abstract

- **Antioxidant amplifies antibiotic protection in the cecal ligation and puncture model of microbial sepsis through interleukin-10 production.**
Author(s): Kotake Y, Moore DR, Vasquez-Walden A, Tabatabaie T, Sang H.
Source: Shock (Augusta, Ga.). 2003 March; 19(3): 252-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12630525&dopt=Abstract

- **Can CAM therapies help reduce antibiotic resistance?**
Author(s): MacKay D.
Source: Alternative Medicine Review : a Journal of Clinical Therapeutic. 2003 February; 8(1): 28-42. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12611559&dopt=Abstract

- **Catalytic properties of an endogenous beta-lactamase responsible for the resistance of Azospirillum lipoferum to beta-lactam antibiotics.**
Author(s): Boggio SB, Roveri OA.
Source: Microbiology (Reading, England). 2003 February; 149(Pt 2): 445-50.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12624206&dopt=Abstract

- **Cross-cultural differences in lay attitudes and utilisation of antibiotics in a Belgian and a Dutch city.**
Author(s): Deschepper R, Vander Stichele RH, Haaijer-Ruskamp FM.
Source: Patient Education and Counseling. 2002 October -November; 48(2): 161-9.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12401419&dopt=Abstract

- **Dacrymenone and VM 3298-2--new antibiotics with antibacterial and antifungal activity.**
Author(s): Mierau V, Anke T, Sterner O.
Source: Z Naturforsch [c]. 2003 July-August; 58(7-8): 541-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12939041&dopt=Abstract

- **Differences in antibiotic resistance in Escherichia coli, isolated from East-European swine herds with or without prophylactic use of antibiotics.**
Author(s): Docic M, Bilkei G.

Source: Journal of Veterinary Medicine. B, Infectious Diseases and Veterinary Public Health. 2003 February; 50(1): 27-30.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12710497&dopt=Abstract

- **Economic evaluation of antibiotic prophylaxis in small-cell lung cancer patients receiving chemotherapy: an EORTC double-blind placebo-controlled phase III study (08923).**
  Author(s): Tjan-Heijnen VC, Caleo S, Postmus PE, Ardizzoni A, Burghouts JT, Buccholz E, Biesma B, Gorlia T, Crott R, Giaccone G, Debruyne C, Manegold C; European Organisation for Research Treatment of Cancer-Lung Cancer Group and Health Economics Unit.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 2003 February; 14(2): 248-57.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12562652&dopt=Abstract

- **Effect of outer-membrane permeabilizers on the activity of antibiotics and plant extracts against Pseudomonas aeruginosa.**
  Author(s): Guha A, Choudhury A, Unni BG, Roy MK.
  Source: Folia Microbiol (Praha). 2002; 47(4): 379-84.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12422514&dopt=Abstract

- **Effects of some plant extracts and antibiotics on Pseudomonas aeruginosa isolated from various burn cases.**
  Author(s): Al-Saimary IE, Bakr SS, Jaffar T, Al-Saimary AE, Salim H, Al-Muosawi R.
  Source: Saudi Med J. 2002 July; 23(7): 802-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12174229&dopt=Abstract

- **Efficacy of saccharomyces boulardii with antibiotics in acute amoebiasis.**
  Author(s): Mansour-Ghanaei F, Dehbashi N, Yazdanparast K, Shafaghi A.
  Source: World Journal of Gastroenterology : Wjg. 2003 August; 9(8): 1832-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12918131&dopt=Abstract

- **Esberitox N as supportive therapy when providing standard antibiotic treatment in subjects with a severe bacterial infection (acute exacerbation of chronic bronchitis). A multicentric, prospective, double-blind, placebo-controlled study.**
  Author(s): Hauke W, Kohler G, Henneicke-Von Zepelin HH, Freudenstein J.
  Source: Chemotherapy. 2002 December; 48(5): 259-66.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12476043&dopt=Abstract

- **Influence of co-administered antibiotics on the pharmacokinetic fate in rats of paeoniflorin and its active metabolite paeonimetabolin-I from Shaoyao-Gancao-tang.**
  Author(s): He JX, Akao T, Tani T.

Source: The Journal of Pharmacy and Pharmacology. 2003 March; 55(3): 313-21.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12724036&dopt=Abstract

- **Interactions of the oral contraceptive pill with antibiotics and St John's work: knowledge of female college students.**
  Author(s): Hindmarch M, Oakeshott P.
  Source: Family Practice. 2002 December; 19(6): 708.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12429683&dopt=Abstract

- **Lactobacillus GG prevents recurrence of colitis in HLA-B27 transgenic rats after antibiotic treatment.**
  Author(s): Dieleman LA, Goerres MS, Arends A, Sprengers D, Torrice C, Hoentjen F, Grenther WB, Sartor RB.
  Source: Gut. 2003 March; 52(3): 370-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12584218&dopt=Abstract

- **Meta-analysis: the effect of probiotic administration on antibiotic-associated diarrhoea.**
  Author(s): Cremonini F, Di Caro S, Nista EC, Bartolozzi F, Capelli G, Gasbarrini G, Gasbarrini A.
  Source: Alimentary Pharmacology & Therapeutics. 2002 August; 16(8): 1461-7. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12182746&dopt=Abstract

- **Molecular characterization of NikD, a new flavoenzyme important in the biosynthesis of nikkomycin antibiotics.**
  Author(s): Venci D, Zhao G, Jorns MS.
  Source: Biochemistry. 2002 December 31; 41(52): 15795-802.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12501208&dopt=Abstract

- **New approaches for anti-infective drug discovery: antibiotics, vaccines and beyond.**
  Author(s): Cheng Q, Wang S, Salyers AA.
  Source: Current Drug Targets. Infectious Disorders. 2003 March; 3(1): 66-75. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12570734&dopt=Abstract

- **Non-antibiotic therapies for infectious diseases.**
  Author(s): Carson CF, Riley TV.
  Source: Commun Dis Intell. 2003; 27 Suppl: S143-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12807291&dopt=Abstract

- **Obtaining antibiotics without a prescription.**
  Author(s): Goff BJ, Koff JM, Geiling JA.

Source: The New England Journal of Medicine. 2002 July 18; 347(3): 223.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12124419&dopt=Abstract

- **Phase I and pharmacokinetic study of docetaxel in combination with epirubicin and cyclophosphamide in advanced cancer: dose escalation possible with granulocyte colony-stimulating factor, but not with prophylactic antibiotics.**
  Author(s): Rischin D, Ackland SP, Smith J, Garg MB, Clarke S, Millward MJ, Toner GC, Zalcberg J.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 2002 November; 13(11): 1810-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12419756&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

- **Probiotics and antibiotic associated diarrhoea. Lactulose is effective.**
  Author(s): Battle M, Teare L, Law S, Fulton J.
  Source: Bmj (Clinical Research Ed.). 2002 October 19; 325(7369): 901; Author Reply 901.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12386048&dopt=Abstract

- **Probiotics and antibiotic associated diarrhoea. The case for probiotics remains unproved.**
  Author(s): Beckly J, Lewis S.
  Source: Bmj (Clinical Research Ed.). 2002 October 19; 325(7369): 901; Author Reply 901.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12395791&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

- **Synergistic effect of ayurvedic pearl preparation on enhancing effectiveness of antibiotics.**
  Author(s): Kulkarni M, Deopujari JY, Purohit HJ.
  Source: Indian J Exp Biol. 2002 July; 40(7): 831-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12597554&dopt=Abstract

- **The efficacy of prophylactic outpatient antibiotics for the prevention of neutropenic fever associated with high-dose etoposide (VP-16) for stem cell mobilization.**
  Author(s): Avery RK, Pohlman BL, Mossad SB, Goormastic M, Longworth DL, Kalaycio ME, Sobecks RM, Andresen SW, Kuczkowski E, Bernhard L, Ostendorf H, Wise K, Bolwell BJ.
  Source: Bone Marrow Transplantation. 2002 September; 30(5): 311-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12209353&dopt=Abstract

- **The European ban on growth-promoting antibiotics and emerging consequences for human and animal health.**
  Author(s): Casewell M, Friis C, Marco E, McMullin P, Phillips I.
  Source: The Journal of Antimicrobial Chemotherapy. 2003 August; 52(2): 159-61. Epub 2003 July 01. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12837737&dopt=Abstract

- **The use of some immunomodulators and non-antibiotic drugs in a prophylaxis and treatment of mastitis.**
  Author(s): Malinowski E.
  Source: Pol J Vet Sci. 2002; 5(3): 197-202. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12448082&dopt=Abstract

- **Treatment of female urethral syndrome refractory to antibiotics.**
  Author(s): Yoon SM, Jung JK, Lee SB, Lee T.
  Source: Yonsei Medical Journal. 2002 October; 43(5): 644-51.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12402379&dopt=Abstract

- **Treatment with Hypericum perforatum L. does not trigger decreased resistance in Staphylococcus aureus against antibiotics and hyperforin.**
  Author(s): Hubner AT.
  Source: Phytomedicine : International Journal of Phytotherapy and Phytopharmacology. 2003 March; 10(2-3): 206-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12725578&dopt=Abstract

- **Use of prostatic massage in combination with antibiotics in the treatment of chronic prostatitis.**
  Author(s): Shoskes DA, Zeitlin SI.

Source: Prostate Cancer and Prostatic Diseases. 1999 May; 2(3): 159-162.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12496826&dopt=Abstract

- **Use of subtherapeutic antibiotics in livestock (as supplements or feed additives) with the induction of resistance in human bacterial pathogens, the magnitude and complexity of the problem become increasingly clear.**
  Author(s): Goldsmith RS, Schur PM.
  Source: Journal of Environmental Health. 2002 October; 65(3): 7, 21.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12369248&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 antibiotics; 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**

  **Abdominal Wall Inflammation**
  Source: Integrative Medicine Communications; www.drkoop.com

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

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

**Acne Rosacea**
Source: Healthnotes, Inc.; www.healthnotes.com

**Acne Vulgaris**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

**Anaphylaxis**
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: 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

**Bone Loss**
Source: Integrative Medicine Communications; www.drkoop.com

**Breast Cancer**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

**Candida/yeast Hypersensitivity Syndrome**
Source: Prima Communications, Inc.www.personalhealthzone.com

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

**Canker Sores**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

**Chronic Venous Insufficiency**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

**Common Cold/sore Throat**
Source: Healthnotes, Inc.; www.healthnotes.com

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

**Conjunctivitis and Blepharitis**
Source: Healthnotes, Inc.; www.healthnotes.com

**Cough**
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

**Cutaneous Drug Reactions**
Source: Integrative Medicine Communications; www.drkoop.com

**Cystic Fibrosis**
Source: Healthnotes, Inc.; www.healthnotes.com

**Cystic Fibrosis**
Source: Integrative Medicine Communications; www.drkoop.com

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

**Dermatitis Herpetiformis**
Source: Healthnotes, Inc.; www.healthnotes.com

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

**Diverticular Disease**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

**Fever of Unknown Origin**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

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

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

**HIV and AIDS Support**
Source: Healthnotes, Inc.; www.healthnotes.com

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

**Hookworm**
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: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

**Lyme Disease**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

**Mitral Valve Prolapse**
Source: Healthnotes, Inc.; www.healthnotes.com

**Nail Disorders**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

**Peptic Ulcer**
Source: Healthnotes, Inc.; www.healthnotes.com

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

**Peripheral Vascular Disease**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

**Pink Eye**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

**Prostate Infection**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

**Pyloric Stenosis**
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

**Recurrent Ear Infections**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

**Sexually Transmitted Diseases**
Source: Integrative Medicine Communications; www.drkoop.com

**Shingles and Postherpetic Neuralgia**
Source: Healthnotes, Inc.; www.healthnotes.com

**Sickle Cell Anemia**
Source: Healthnotes, Inc.; www.healthnotes.com

**Sinus Congestion**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

**Skin Infection**
Source: Integrative Medicine Communications; www.drkoop.com

**Sore Throat**
Source: Integrative Medicine Communications; www.drkoop.com

**Spontaneous Abortion**
Source: Integrative Medicine Communications; www.drkoop.com

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

**Stomach Inflammation**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

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

**Urethral Inflammation**
Source: Integrative Medicine Communications; www.drkoop.com

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

**Urinary Incontinence**
Source: Integrative Medicine Communications; www.drkoop.com

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

**Urinary Tract Infection in Women**
Source: Integrative Medicine Communications; www.drkoop.com

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

**Vaginal Inflammation**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

**Varicose Veins**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

**Whooping Cough**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

- **Alternative Therapy**

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

Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,669,00.html

**Native American Medicine**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,721,00.html

**Naturopathy**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,722,00.html

- **Herbs and Supplements**

**Acidophilus and Other Probiotics**
Source: Prima Communications, Inc.www.personalhealthzone.com

**Aesculus**
Alternative names: Horse Chestnut; Aesculus hippocastanum L.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

**Allium Sativum**
Source: Integrative Medicine Communications; www.drkoop.com

**Alpha-lipoic Acid**
Source: Integrative Medicine Communications; www.drkoop.com

**Aminoglycoside Antibiotics**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

**Amoxicillin**
Alternative names: Amoxil, Trimox, Wymox
Source: Prima Communications, Inc.www.personalhealthzone.com

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

**Ananas Comosus**
Alternative names: Bromelain
Source: Integrative Medicine Communications; www.drkoop.com

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

**Anti-infective Agents**
Source: Healthnotes, Inc.; www.healthnotes.com

**Antitubercular Agents**
Source: Healthnotes, Inc.; www.healthnotes.com

**Antituberculosis Agents**
Source: Integrative Medicine Communications; www.drkoop.com

**Arctostaphylos Uva Ursi**
Source: Integrative Medicine Communications; www.drkoop.com

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

**Barberry**
Alternative names: Berberis vulgaris, Berberry
Source: Integrative Medicine Communications; www.drkoop.com

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

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

**Bee Products**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,756,00.html

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

**Berberis Vulgaris**
Source: Integrative Medicine Communications; www.drkoop.com
**Berberry**
Source: Integrative Medicine Communications; www.drkoop.com

**Bismuth Subsalicylate**
Source: Healthnotes, Inc.; www.healthnotes.com

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

**Bovine Colostrum**
Source: Healthnotes, Inc.; www.healthnotes.com

**Brewer's Yeast**
Source: Healthnotes, Inc.; www.healthnotes.com

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

**Bromelain**
Alternative names: Ananas comosus
Source: Integrative Medicine Communications; www.drkoop.com

**Bromelainum**
Alternative names: Bromelain
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

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

**Centella**
Alternative names: Gotu Kola; Centella asiatica (Linn.)
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

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

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

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

**Chlorhexidine**
Source: Healthnotes, Inc.; www.healthnotes.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

**Cobalamin**
Alternative names: Vitamin B12 (Cobalamin)
Source: Integrative Medicine Communications; www.drkoop.com

**Colloidal Silver**
Source: Healthnotes, Inc.; www.healthnotes.com

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

**Cranberry**
Alternative names: Vaccinium macrocarpon
Source: Healthnotes, Inc.; www.healthnotes.com

**Cranberry**
Alternative names: Vaccinium macrocarpon
Source: Integrative Medicine Communications; www.drkoop.com

**Cranberry**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10019,00.html

**Curcuma Longa**
Source: Integrative Medicine Communications; www.drkoop.com

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

**Dandelion**
Alternative names: Taraxacum officinale
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

**Dryopteris**
Alternative names: Male Fern; Dryopteris sp.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

**Echinacea**
Alternative names: Echinacea angustifolia, Echinacea pallida, Echinacea purpurea, Purple Coneflower
Source: Integrative Medicine Communications; www.drkoop.com

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

**Echinacea**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,775,00.html

**Echinacea Angustifolia**
Source: Integrative Medicine Communications; www.drkoop.com

**Echinacea Pallida**
Source: Integrative Medicine Communications; www.drkoop.com

**Echinacea Purpurea**
Source: Integrative Medicine Communications; www.drkoop.com

**Edta**
Alternative names: Ethylenediaminetetraacetic Acid (EDTA)
Source: Integrative Medicine Communications; www.drkoop.com

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

**Ethylenediaminetetraacetic Acid (edta)**
Alternative names: EDTA
Source: Integrative Medicine Communications; www.drkoop.com

**Eucalyptus**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,778,00.html

**Eugenia Clove**
Alternative names: Cloves; Eugenia sp.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

**Gamma-linolenic Acid (gla)**
Alternative names: GLA
Source: Integrative Medicine Communications; www.drkoop.com

**Garcinia Sp**
Alternative names:.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

**Gla**
Alternative names: Gamma-Linolenic Acid (GLA)
Source: Integrative Medicine Communications; www.drkoop.com

**Glandular Extracts**
Source: Healthnotes, Inc.; www.healthnotes.com

**Glycyrrhiza1**
Alternative names: Licorice; Glycyrrhiza glabra L.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

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

**Goldenseal**
Alternative names: Hydrastis canadensis
Source: Healthnotes, Inc.; www.healthnotes.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

**Grapefruit Seed Extract**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

**Green Tea**
Source: Prima Communications, Inc.www.personalhealthzone.com

**Herbal Decongestant**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,949,00.html

**Horseradish**
Alternative names: Cochlearia armoracia
Source: Healthnotes, Inc.; www.healthnotes.com

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

**L. Acidophilus**
Source: Integrative Medicine Communications; www.drkoop.com

**Lactobacillus Acidophilus**
Source: Integrative Medicine Communications; www.drkoop.com

**Lavandula**
Alternative names: Lavender; Lavandula sp.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

**Lepidium Sp**
Alternative names: Cress; Lepidium sp.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

**Loracarbef**
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

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

**Menadione**
Alternative names: Vitamin K
Source: Integrative Medicine Communications; www.drkoop.com

**Menaphthone**
Alternative names: Vitamin K
Source: Integrative Medicine Communications; www.drkoop.com

**Menaquinone**
Alternative names: Vitamin K
Source: Integrative Medicine Communications; www.drkoop.com

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

**Metronidazole (vaginal)**
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

**Ocimum**
Alternative names: Basil, Albahaca; Ocimum basilicum
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

**Origanum**
Alternative names: Oregano; Origanum vulgare
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

**Paba**
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

**Paba (para-aminobenzoic Acid)**
Source: Prima Communications, Inc.www.personalhealthzone.com

**Passiflora**
Alternative names: Passion Flower; Passiflora alata L.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

**Penicillamine**
Source: Healthnotes, Inc.; www.healthnotes.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

**Phylloquinone**
Alternative names: Vitamin K
Source: Integrative Medicine Communications; www.drkoop.com

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

**Psyllium**
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,814,00.html

**Purple Coneflower**
Source: Integrative Medicine Communications; www.drkoop.com

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

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

**St. John's Wort**
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

**Taraxacum Officinale**
Alternative names: Dandelion
Source: Integrative Medicine Communications; www.drkoop.com
**Tea Tree**
Alternative names: Melaleuca alternifolia
Source: Healthnotes, Inc.; www.healthnotes.com

**Tea Tree**
Source: Prima Communications, Inc.www.personalhealthzone.com

**Terminalia**
Alternative names: Myrobalans; Terminalia arjuna
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

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

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

**Thuja Plicata**
Alternative names: Western Red Cedar
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

**Thymus**
Alternative names: Thyme; Thymus vulgaris
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

**Topical Corticosteroids**
Source: Healthnotes, Inc.; www.healthnotes.com

**Tribulus Puncture**
Alternative names: Puncture Vine, Goathead; Tribulus terrestris L.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

**Trimethoprim/sulfamethoxazole**
Source: Healthnotes, Inc.; www.healthnotes.com

**Trimethoprim/sulfamethoxazole**
Alternative names: Bactrim, Cotrim, Septra, Sulfatrim
Source: Prima Communications, Inc.www.personalhealthzone.com

**Turmeric**
Alternative names: Curcuma longa
Source: Integrative Medicine Communications; www.drkoop.com

**Usnea**
Alternative names: Usnea barbata
Source: Healthnotes, Inc.; www.healthnotes.com

**Uva Ursi**
Alternative names: Arctostaphylos uva ursi, Bearberry, Beargrape
Source: Integrative Medicine Communications; www.drkoop.com

**Uva Ursi**
Source: Prima Communications, Inc.www.personalhealthzone.com

**Vaccinium Macrocarpon**
Source: Integrative Medicine Communications; www.drkoop.com

**Vitex**
Alternative names: Chaste; Vitex agnus-castus
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

**Withania Ashwagandha**
Alternative names: Ashwagandha; Withania somnifera L.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

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

## General References

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

# CHAPTER 4. DISSERTATIONS ON ANTIBIOTICS

## Overview

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

## Dissertations on Antibiotics

*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 antibiotics. 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:

- **30s Ribosomal Subunit Assembly Is a Target for Inhibition by Aminoglycoside Antibiotics in Escherichia Coli** by Mehta, Roopal Manoj; Ms from East Tennessee State University, 2002, 30 pages
  http://wwwlib.umi.com/dissertations/fullcit/1408232
- **A Medical Office-based, Parent-focused Intervention to Reduce Overprescribing Antibiotics to Children** by Alder, Stephen Craig; Phd from The University of Utah, 2001, 186 pages
  http://wwwlib.umi.com/dissertations/fullcit/3028665
- **A Study of Aminoglycoside Antibiotic-rna Interactions** by Wu, Jui-yu; Phd from Wayne State University, 2002, 216 pages
  http://wwwlib.umi.com/dissertations/fullcit/3071849

- **Aldo-keto, Azidodeoxy and Deoxy Sugars New Synthetic Routes to the Carbohydrate Moieties of Antibiotics** by Lawton, Brian Thomas; Advdeg from Queen's University at Kingston (canada), 1969
http://wwwlib.umi.com/dissertations/fullcit/NK03430
- **Antibiotic Animal Feed Additives and Public Policy: Farm Operators' Beliefs about the Importance of These Additives and Their Attitudes toward Government Regulation of Agricultural Chemicals and Pharmaceuticals (new York)** by Gillespie, Gilbert Wayne, Jr., Phd from Cornell University, 1987, 417 pages
http://wwwlib.umi.com/dissertations/fullcit/8708936
- **Antibiotic Resistance in Campylobacter Jejuni: Molecular Mechanisms, Dynamics of Emergence, and Ecological Fitness in Poultry** by Luo, Naidan; Phd from The Ohio State University, 2002, 189 pages
http://wwwlib.umi.com/dissertations/fullcit/3059294
- **Antibiotic Use and the Risk of Breast Cancer** by Velicer, Christine Marie; Phd from University of Washington, 2003, 73 pages
http://wwwlib.umi.com/dissertations/fullcit/3091087
- **Antibiotic-resistant Bacteria in Ready-to-eat Shrimp** by Duran, Gianna Marcella; Ms from Mississippi State University, 2003, 87 pages
http://wwwlib.umi.com/dissertations/fullcit/1413235
- **Antibiotics and Organic Acids As Modulators of Whole-body and Visceral Organ Growth in the 14-day Weaned Piglet** by Borysenko, Michelle Kathleen; Msc from University of Guelph (canada), 2002, 199 pages
http://wwwlib.umi.com/dissertations/fullcit/MQ71191
- **Antibiotics from Erwinia Herbicola** by Jin, Mi; Phd from Cornell University, 2003, 152 pages
http://wwwlib.umi.com/dissertations/fullcit/3075892
- **Approaches to the Synthesis of Antibiotics Amino Sugars** by Georges, Fawzy, F. Z; Phd from University of Ottawa (canada), 1977
http://wwwlib.umi.com/dissertations/fullcit/NK33689
- **Bacterial and Pharmacological Factors That Influence the Selection of Antibiotic Resistance** by Gustafsson, Ingegerd; Phd from Uppsala Universitet (sweden), 2003, 49 pages
http://wwwlib.umi.com/dissertations/fullcit/f27057
- **Chemical Methods for Studying the Biosynthesis of Lantibiotics and Prostaglandins** by Okeley, Nicole Marie; Phd from University of Illinois at Urbana-champaign, 2002, 151 pages
http://wwwlib.umi.com/dissertations/fullcit/3044191
- **Demethyl (c-11) Cezomycin: a Novel Calcimycin Antibiotic from the Symbiotic, Dinitrogen-fixing Actinomycete Frankia** by Haansuu, Johannes Pasi; Phd from Helsingin Yliopisto (finland), 2002, 74 pages
http://wwwlib.umi.com/dissertations/fullcit/f335585
- **Developing Methodology for the Total Synthesis of Oxazole-triene Antibiotics** by Nguyen, Hanh Nho; Phd from University of Michigan, 2003, 202 pages
http://wwwlib.umi.com/dissertations/fullcit/3079510

- **Differences in Use of Antibiotics between Flanders and the Netherlands: a Comparative Anthropological Study of the Lay Perspective (belgium)** by Deschepper, Reginald; from Rijksuniversiteit Te Gent (belgium), 2002, 300 pages
  http://wwwlib.umi.com/dissertations/fullcit/f281329
- **Disinfectant- and Antibiotic Resistant Bacteria from Food and Clinical Environments** by Sidhu, Maan Singh; Drscient from Norges Landbrukshogskole (norway), 2002, 165 pages
  http://wwwlib.umi.com/dissertations/fullcit/f336097
- **Economics of Antibiotic Resistance** by Laxminarayan, Ramanan; Phd from University of Washington, 1999, 127 pages
  http://wwwlib.umi.com/dissertations/fullcit/9952858
- **Effect of Antibiotics on Blood Lipids** by Hamidi, Maryam; Msc from University of Toronto (canada), 2002, 91 pages
  http://wwwlib.umi.com/dissertations/fullcit/MQ68802
- **Effects of Diet and Antibiotics on Ruminal Fermentation and Subacute Acidosis in Cattle** by Ives, Samuel Engler; Phd from Kansas State University, 2002, 117 pages
  http://wwwlib.umi.com/dissertations/fullcit/3052582
- **Effects of Patient Persuasion on Physician Prescribing of Antibiotics** by Yaldo, Avin Z.; Phd from University of Florida, 2002, 111 pages
  http://wwwlib.umi.com/dissertations/fullcit/3056797
- **Epidemiology of Enterococci with Acquired Resistance to Antibiotics in Sweden: Special Emphasis on Ampicillin and Vancomycin** by Torell, Erik Gunnar; Phd from Uppsala Universitet (sweden), 2003, 80 pages
  http://wwwlib.umi.com/dissertations/fullcit/f148497
- **Evaluation of Growth Enhancement Antibiotics and Possible Alternatives in Broiler Diets** by Roberts, Copie Denise; Ms from Stephen F. Austin State University, 2002, 80 pages
  http://wwwlib.umi.com/dissertations/fullcit/1410007
- **Glycosyltransferases Involved in the Biosynthesis of Glycopeptide Antibiotics** by Losey, Heather Christina; Phd from Harvard University, 2003, 166 pages
  http://wwwlib.umi.com/dissertations/fullcit/3076905
- **Mechanisms of Resistance to Macrolide, Lincosamide and Streptogramin Antibiotics in Streptococcus and Enterococcus (spanish Text)** by Portillo Barrio, Aranzazu; Dr from Universidad De La Rioja (spain), 2002, 245 pages
  http://wwwlib.umi.com/dissertations/fullcit/3086671
- **Microbial Source Tracking Using F(+)rna Coliphage Typing and Escherichia Coli Antibiotic Resistance Assays** by Stewart, Jill Rene; Phd from The University of North Carolina at Chapel Hill, 2003, 210 pages
  http://wwwlib.umi.com/dissertations/fullcit/3086628
- **Modifications of Radiation-induced Mutation Frequencies by Antibiotics in Drosophila Melanogaster** by Mukherjee, R. N; Advdeg from The University of British Columbia (canada), 1965
  http://wwwlib.umi.com/dissertations/fullcit/NK00184

- **Negotiating Antibiotic Treatment in Pediatric Care: the Communication of Preferences in Physician-parent Interaction** by Stivers, Tanya Jean; Phd from University of California, Los Angeles, 2000, 405 pages
http://wwwlib.umi.com/dissertations/fullcit/9979038
- **New Antibiotics from a Marine Isolate of Bacillus Laterosporus** by Barsby, Todd Alan; Phd from The University of British Columbia (canada), 2002, 210 pages
http://wwwlib.umi.com/dissertations/fullcit/NQ74992
- **Pharmacoepidemiology of Antibiotics, Weak Opioids and Statins with Special Reference to Socioeconomic Aspects: an Ecological Approach** by Henricson, Karin Ann-charlotte; Drmedsci from Lunds Universitet (sweden), 2003, 114 pages
http://wwwlib.umi.com/dissertations/fullcit/f155393
- **Production of Antibiotics by Immobilized Cell Bioreactors** by Deo, Yashwant M; Phd from University of Calgary (canada), 1982
http://wwwlib.umi.com/dissertations/fullcit/NK63291
- **Strategies for the Synthesis of the Oxo Polyene Macrolide Antibiotics. Application to the Total Synthesis of Rk-397 and Dermostatin a** by Mitton-fry, Mark Joseph; Phd from University of Colorado at Boulder, 2002, 331 pages
http://wwwlib.umi.com/dissertations/fullcit/3074779
- **Structural and Functional Characterization of the Lantibiotic Mutacin 1140** by Smith, James Leif; Phd from University of Florida, 2002, 159 pages
http://wwwlib.umi.com/dissertations/fullcit/3069045
- **Studies toward the Total Synthesis of Naphthyridinomycin/bioxalomycin Antitumor Antibiotics** by Hopkins, Corey Raymond; Phd from University of Pittsburgh, 2002, 236 pages
http://wwwlib.umi.com/dissertations/fullcit/3054288
- **Syntheses Related to Carbohydrate-containing Antibiotics** by Chen, Lu-yu; Phd from Queen's University at Kingston (canada), 1977
http://wwwlib.umi.com/dissertations/fullcit/NK34594
- **Synthesis of Compounds Related to the Kinamycin Antibiotics** by Laufer, Radoslaw; Phd from University of Waterloo (canada), 2002, 277 pages
http://wwwlib.umi.com/dissertations/fullcit/NQ77239
- **Synthesis of Some New Beta-lactam Antibiotics** by Ugolini, Antonio; Phd from Mcgill University (canada), 1981
http://wwwlib.umi.com/dissertations/fullcit/NK54926
- **Synthetic Studies on Polyether Antibiotics: New Approaches to Oligo-tetrahydrofurans and Complex Spiroketals** by Dabideen, Darrin Rajesh; Phd from City University of New York, 2003, 200 pages
http://wwwlib.umi.com/dissertations/fullcit/3074643
- **The Analysis and Chemistry of Antibiotics and Amines in Model Environmental Systems** by Sithole, Bishop Bruce; Phd from Dalhousie University (canada), 1984
http://wwwlib.umi.com/dissertations/fullcit/NK66087
- **The Behavior of Broad Spectrum Antibiotics Prices 1951-1960: an Economic Analysis.** by Albertine, John Michael, Phd from University of Virginia, 1975, 114 pages
http://wwwlib.umi.com/dissertations/fullcit/7522147
- **The Effects of Cyclopropane Rings, Sterols and Antibiotics on the Structure and Dynamics of Phospholipid Membranes a Deuterium Solid State Nuclear Magnetic**

**Resonance Approach** by Dufourc, Erick Joël; Phd from University of Ottawa (canada), 1983
http://wwwlib.umi.com/dissertations/fullcit/NK65706

- **The Epidemiology of Antibiotic Utilisation: a Study of Antibiotic Use in Institutional Settings and Community Practice** by Jelinski, Susan Elizabeth; Phd from Memorial University of Newfoundland (canada), 2002, 176 pages
http://wwwlib.umi.com/dissertations/fullcit/NQ73552
- **The Evolution of Antibiotic Resistance** by Barlow, Miriam; Phd from The University of Rochester, 2003, 149 pages
http://wwwlib.umi.com/dissertations/fullcit/3074517
- **The Isolation and Antibiotic Resistance Patterns of Staphylococcus from the Skin of Humans and Livestock Using Novobiocin Salt Sucrose Nitrate Medium** by Jetton, Thomas Audie Neal; Ms from Angelo State University, 2002, 40 pages
http://wwwlib.umi.com/dissertations/fullcit/1409770
- **The Mechanism of Porin-mediated Antibiotic Resistance in Neisseria Gonorrhoeae** by Olesky, Melanie; Phd from The University of North Carolina at Chapel Hill, 2002, 191 pages
http://wwwlib.umi.com/dissertations/fullcit/3061709
- **The Process of Antibiotic Prescribing for Acute Respiratory Infections in a Rural Western Community** by Hart, Ann Marie; Phd from University of Colorado Health Sciences Center, 2003, 87 pages
http://wwwlib.umi.com/dissertations/fullcit/3086278
- **The Site of Action of Certain Antibiotics on Neuromuscular Transmission** by Wright, James M; Phd from Mcgill University (canada), 1976
http://wwwlib.umi.com/dissertations/fullcit/NK31921
- **Thiols, Radicals and Antibiotics: Mechanistic Studies in Coenzyme a Biosynthesis** by Strauss, Erick; Phd from Cornell University, 2003, 182 pages
http://wwwlib.umi.com/dissertations/fullcit/3075866
- **Trips and the Pharmaceutical Industry in India: a Case Study of the Antibiotic Sector** by Law, Pia; Phd from Tulane University, 1999, 165 pages
http://wwwlib.umi.com/dissertations/fullcit/9948226

## 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 ANTIBIOTICS

## Overview

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

## Recent Trials on Antibiotics

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

- **A study to determine if antibiotics prevent infection in the pancreas of patients where part of the pancreas has died.**

  Condition(s): Pancreatitis, Acute Necrotizing

  Study Status: This study is currently recruiting patients.

  Sponsor(s): AstraZeneca

  Purpose - Excerpt: This is a research study in patients having a condition known as necrotizing pancreatitis. This is inflammation of the pancreas (an intestinal organ which assists with digestion) that has resulted in the damage and death of some pancreatic tissue. This damaged pancreatic tissue may develop a bacterial infection, which can cause further -sometimes very serious- health problems. It may be possible to prevent or delay infection by giving 'prophylactic' antibiotics (that is - to provide protection before any infection starts). However, it is not certain that this antibiotic therapy will be successful. This study is being carried out to see whether the antibiotic 'Meropenem' (which is also known as MERREM I.V.) provides protection from developing a pancreatic infection. This will be done by comparing the progress of patients who receive meropenem with those who receive a non-active placebo solution (a solution that does not contain any active medication). Meropenem or placebo would be given in addition to the standard treatment received for pancreatitis. It is not known if meropenem will help prevent infections associated with necrotizing pancreatitis. Approximately 240 patients will take part in this study. Study participation will be

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

carried out for up to 6 weeks, and patients will receive the study treatment up to a maximum of 21 days.

Phase(s): Phase IV

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00061438

- **Antibiotic Therapy in Preventing Early Infection in Patients With Multiple Myeloma Who Are Receiving Chemotherapy**

  Condition(s): stage I multiple myeloma; stage II multiple myeloma; stage III multiple myeloma; Infection

  Study Status: This study is currently recruiting patients.

  Sponsor(s): James P. Wilmot Cancer Center; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Giving **antibiotics** may be effective in preventing or controlling early infection in patients with multiple myeloma and may improve their response to chemotherapy. PURPOSE: Randomized clinical trial to compare the effectiveness of **antibiotics** or no **antibiotics** for the prevention of early infection in treating patients with multiple myeloma.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002850

- **Antibiotic treatment for patients with infections of short term in-dwelling vascular catheters due to a specific bacteria (gram positive bacteria)**

  Condition(s): Bacterial Infections; Gram-Positive Bacterial Infections; Bacteremia

  Study Status: This study is currently recruiting patients.

  Sponsor(s): (Sponsor Name Pending)

  Purpose - Excerpt: This study will treat patients who have a short term central catheter that is thought to be infected with a specific bacteria (gram positive bacteria)

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00037050

- **Antibiotic treatment trial directed against Chlamydia pneumonia in multiple sclerosis**

  Condition(s): Multiple Sclerosis

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Center for Research Resources (NCRR); National Multiple Sclerosis Society

  Purpose - Excerpt: Multiple sclerosis (MS) is an inflammatory, demyelinating disease which affects the central nervous system (CNS). The etiology of MS is unknown, although the immune system appears to play a role. Many different infectious agents

have been proposed as potential causes for MS, including Epstein-Barr virus, human herpesvirus 6, and coronaviruses. Recently Dr. Sriram at Vanderbilt University has found evidence for active Chlamydia pneumonia infection in the CNS of MS patients. These findings have been replicated in part by other laboratories. The purpose of the current study is to test whether **antibiotic** treatment aimed at eradicating Chlamydia infection will reduce the disease activity in MS. The primary outcome measure will be reduction in new enhancing MS lesions on brain MRI. Forty patients will be entered into the trial. To be eligible, patients must have evidence of chlamydia infection in their spinal fluid and enhancing lesions on their pre-randomization MRI scans. Patients who meet these criteria will be randomized to either placebo or **antibiotic** therapy, and followed for 6 months on treatment.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00043264

- **New antibiotic to treat pediatric patients with infections due to a specific bacteria (Vancomycin-Resistant Enterococcus)**

  Condition(s): Drug Resistance, Microbial; Bacterial Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): (Sponsor Name Pending)

  Purpose - Excerpt: This study will treat pediatric patients who have infections that are due to a specific bacteria (Vancomycin-Resistant Enterococcus)

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00035854

- **Antibiotic Therapy With or Without G-CSF in Treating Children With Neutropenia and Fever Caused by Chemotherapy**

  Condition(s): unspecified childhood solid tumor, protocol specific; fever, sweats, and hot flashes; Neutropenia

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): Children's Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: **Antibiotics** may decrease the side effects of neutropenia and fever caused by chemotherapy. Colony-stimulating factors such as G-CSF may increase the number of immune cells found in bone marrow or peripheral blood and may help a person's immune system recover from the side effects of chemotherapy. It is not yet known whether **antibiotic** therapy plus G-CSF is more effective than **antibiotic** therapy alone for treating side effects caused by chemotherapy. PURPOSE: Randomized phase III trial to compare the effectiveness of **antibiotic** therapy with or without G-CSF in treating children who have neutropenia and fever that are caused by chemotherapy.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00003739

- **Antibiotics to Reduce Chorioamnionitis-Related Perinatal HIV Transmission**

  Condition(s): HIV Infections

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Child Health and Human Development (NICHD); National Institute of Allergy and Infectious Diseases (NIAID); National Institutes of Health (NIH); National Institute of Mental Health (NIMH); National Institute on Drug Abuse (NIDA)

  Purpose - Excerpt: The purpose of this study is to see if antibiotic drugs given to treat an infection of the uterus during pregnancy can reduce the chances of HIV being passed from an HIV-positive mother to her baby. A link between bacterial disease of the vagina, premature birth, infection of the uterus during pregnancy, and the passing of HIV from a mother to her baby has been found. Early treatment of these problems may reduce the risk of passing HIV from an HIV-positive mother to her baby. [Note: As of 02/21/03, enrollment into this study was halted because preliminary data showed that the study antibiotics were not effective in preventing mother-to-child HIV transmission.]

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00021671

- **A Study of GT160-246 Versus Vancomycin in Patients with Clostridium difficile-Associated Diarrhea**

  Condition(s): Clostridium difficile-Associated Diarrhea; Clostridium Enterocolitis; Clostridium Difficile Diarrhea; Antibiotic-Associated Colitis; Antibiotic-Associated Diarrhea

  Study Status: This study is completed.

  Sponsor(s): Genzyme Drug Discovery and Development

  Purpose - Excerpt: Approximately 300 patients will be entered into this study taking place throughout the United States, Canada and the United Kingdom. This study aims to determine if an investigational drug is safe and effective for treating the symptoms of C. difficile-associated diarrhea and lowering the risk of repeat episodes of diarrhea. The investigational drug will be evaluated in comparison to current standard **antibiotic** treatment, so all patients will receive active medication. All study-related care is provided including doctor visits, physical exams, laboratory tests and study medication. Total length of participation is approximately 10 weeks.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00034294

- **Antibiotic treatment of Gulf War Veterans' illnesses**

  Condition(s): Persian Gulf Syndrome; Mycoplasma fermentans

  Study Status: This study is completed.

Sponsor(s): Department of Veterans Affairs; Department of Veterans Affairs Cooperative Studies Program; Pfizer; Department of Defense

Purpose - Excerpt: In 1990 and 1991, the U.S. deployed approximately 700,000 troops to the Persian Gulf to liberate Kuwait from Iraqi occupation. While there were few casualties associated with the Gulf War, many individuals returned from this conflict with unexplained symptoms and illnesses. This constellation of symptoms has been termed Gulf War Veterans' Illnesses (GWI). Although several explanations have been offered as to the cause of GWI, none of the putative etiologic agents or conditions is currently supported by sufficient evidence. One explanation that has received fairly widespread attention is systemic Mycoplasma fermentans infection. It is the purpose of this study to determine if **antibiotic** treatment directed against Mycoplasma species (i.e. doxycycline) will improve functioning and symptoms in deployed Gulf War veterans with GWI.

Phase(s): Phase III

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00007735

- **Antibiotics in Infancy--Risk Factor for Childhood Asthma**

  Condition(s): Asthma; Lung Diseases

  Study Status: This study is completed.

  Sponsor(s): National Heart, Lung, and Blood Institute (NHLBI)

  Purpose - Excerpt: To examine possible relationships between antibiotic use, as determined by prescriptions filled, and asthma in children ages 6 to 7.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00037726

- **New Antibiotic to treat patients with community-acquired pneumonia due to a specific bacteria (S. pneumoniae pneumonia)**

  Condition(s): Pneumonia, Pneumococcal; Community Acquired Infections; Gram-Positive Bacterial Infections

  Study Status: This study is completed.

  Sponsor(s): (Sponsor Name Pending)

  Purpose - Excerpt: This study will treat patients who have a community-acquired pneumonia that is due to a specific bacteria (S. pneumoniae)

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00035269

## 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 "antibiotics" (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 ANTIBIOTICS

## 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 "antibiotics" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on antibiotics, we have not necessarily excluded non-medical patents in this bibliography.

## Patents on Antibiotics

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

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

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

- **2-substituted piperidine analogs and their use as subtype-selective NMDA receptor antagonists**

  Inventor(s): Bigge; Christopher F. (Ann Arbor, MI), Cai; Sui Xiong (Foothill, CA), Guzikowski; Anthony P. (Eugene, OR), Keana; John F. W. (Eugene, OR), Lan; Nancy C. (South Pasadena, CA), Weber; Eckard (Laguna Beach, CA), Woodward; Richard (Aliso Viejo, CA)

  Assignee(s): Cocensys, Inc. (Irvine, CA), Warner-Lambert & Company (Morris Plains, NJ)

  Patent Number: 6,534,525

  Date filed: June 21, 2000

  Abstract: Novel 2-substituted piperidine analogs, pharmaceutical compositions containing the same and the method of using 2-substituted piperidine analogs as selectively active antagonist of N-methyl-D-aspartate (NMDA) receptor subtypes for treating conditions such as stroke, cerebral ischemia, central nervous system trauma, hypoglycemia, anxiety, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine headaches, chronics pain, glaucoma, CMV retinitis, psychosis, urinary incontinence, opioid tolerance or withdrawal, or neurodegenerative disorders, such as lathyrism, Alzheimer's Disease, Parkinsonism and Huntington's Disease are described.

  Excerpt(s): This invention is related to 2-substituted piperidine analogs. The analogs are selectively active as antagonists of N-methyl-D-aspartate (NMDA) receptor subtypes. The invention is also directed to the use of 2-substituted piperidine analogs as neuroprotective agents for treating conditions such as stroke, cerebral ischemia, central nervous system trauma, hypoglycemia, anxiety, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine headaches, chronic pain, glaucoma, CMV retinitis, psychosis, urinary incontinence, opioid tolerance or withdrawal, or neuro-degenerative disorders such as lathyrism, Alzheimer's Disease, Parkinsonism and Huntington's Disease. Excessive excitation by neurotransmitters can cause the degeneration and death of neurons. It is believed that this degeneration is in part mediated by the excitotoxic actions of the excitatory amino acids (EAA) glutamate and aspartate at the N-methyl-D-Aspartate (NMDA) receptor. This excitotoxic action is considered responsible for the loss of neurons in cerebrovascular disorders such as cerebral ischemia or cerebral infarction resulting from a range of conditions, such as thromboembolic or hemorrhagic stroke, cerebral vasospasms, hypoglycemia, cardiac arrest, status epilepticus, perinatal asphyxia, anoxia such as from drowning, pulmonary surgery and cerebral trauma, as well as lathyrism, Alzheimer's Disease, Parkinson's Disease and Huntington's Disease. wherein Ar represents a phenyl group substituted by R.sub.2, R.sub.3 and R.sub.4 or a naphth-1-yl or naphth-2-yl group, substituted or unsubstituted by 1 or 2 halogen atoms; X represents an oxygen atom or sulfur atom; R.sub.1 represents H or a halogen atom; R.sub.2 represents a halogen atom, a trifluoromethyl group, a phenyl group which is unsubstituted or substituted by 1 to 3 halogen atoms, a phenoxy group which is unsubstituted or substituted by 1 to 3 halogen atoms, or a C.sub.1 -C.sub.4 alkyl group and the benzyl group substitutes the piperidine radical in the 2, 3 or 4 position. This reference does not exemplify. 2-substituted piperidines. The piperidines are said to be useful as antimicrobial agents, but there is no disclosure or suggestion of treating disorders responsive to selective NMDA receptor subtype antagonists.

Web site: http://www.delphion.com/details?pn=US06534525__

- **Acyl phosphonate inhibitors of.beta.-lactamases**

  Inventor(s): Besterman; Jeffrey M. (Baie d'Urfe, CA), Pratt; Rex (Portland, CT), Rahil; Jubrail (Dollard des Ormeaux, CA)

  Assignee(s): MethylGere, Inc. (St. Laurent, CA)

  Patent Number: 6,599,889

  Date filed: March 1, 2001

  Abstract: The invention provides novel.beta.-lactamase inhibitors, which are structurally unrelated to the natural product and semi-synthetic.beta.-lactamase inhibitors presently available, and which do not possess a.beta.-lactam pharmacophore. These new inhibitors are fully synthetic, allowing ready access to a wide variety of structurally related analogs. Certain embodiments of these new inhibitors also bind bacterial DD-peptidases, thus potentially acting both as.beta.-lactamase inhibitors and as **antibiotics.**

  Excerpt(s): The invention relates to bacterial **antibiotic** resistance. More particularly, the invention relates to compositions and methods for overcoming bacterial **antibiotic** resistance. Bacterial **antibiotic** resistance has become one of the most important threats to modern health care. Cohen, Science 257:1051-1055 (1992) discloses that infections caused by resistant bacteria frequently result in longer hospital stays, higher mortality and increased cost of treatment. Neu, Science 257:1064-1073 (1992) discloses that the need for new **antibiotics** will continue to escalate because bacteria have a remarkable ability to develop resistance to new agents rendering them quickly ineffective. The present crisis has prompted various efforts to elucidate the mechanisms responsible for bacterial resistance. Coulton et al. Progress in Medicinal Chemistry 31:297-349 (1994) teach that the widespread use of penicillins and cephalosporins has resulted in the emergence of.beta.-lactamases, a family of bacterial enzymes that catalyze the hydrolysis of the.beta.-lactam ring common to presently used **antibiotics.** More recently, Dudley, Pharmacotherapy 15: 9S14S (1995) has disclosed that resistance mediated by.beta.-lactamases is a critical aspect at the core of the development of bacterial **antibiotic** resistance.

  Web site: http://www.delphion.com/details?pn=US06599889__

- **Antibacterial composition for control of gram positive bacteria in food applications**

  Inventor(s): King; William (Walnut Creek, CA), Ming; Xintian (Cottage Grove, WI)

  Assignee(s): Rhodia, Inc. (Cranbury, NJ)

  Patent Number: 6,620,446

  Date filed: July 10, 2002

  Abstract: An antibacterial composition comprising: (a) a first component including at least one gram positive bacteristatic or bactericidal compound selected from the group consisting of: **antibiotics,** pediocin, and lacticin class bacteriocins, and lytic enzymes; and (b) a second component including at least one compound selected from the group consisting of hops acids, or hops acid derivatives, hops resin; and hops resin derivatives; and the method of applying said composition to the surfaces of solid food.

Excerpt(s): The present invention discloses a process for inhibiting or retarding the outgrowth of bacteria on food products by treatment with a composition which includes one or more hops acid extracts or modified hops acid extracts plus one or more safe and suitable gram positive bacteristatic or bactericidal preparations from the lantibiotics, pediocin, lacticin class bacteriocin and/or lytic enzyme categories. More specifically, the process comprises using as an ingredient or applying to a food surface a composition including nisin, and/or lysozyme and beta hops acids in order to reduce or eliminate gram positive spoilage or pathogenic bacteria, and, most especially, all strains of the harmful pathogen Listeria monocytogenes. An important public health concern is the ability of pathogenic listerial species, especially Listeria monocytogenes, to grow at commercial refrigeration temperatures at which processed foods are normally stored for long periods of time. This ability to grow under standard conditions of distribution makes Listeria monocytogenes one of the top public health risks associated with raw and processed foods today. Any new antimicrobial system must be effective in commercial food systems, with formulation and temperature conditions reflecting actual practices. The new compositions of this patent are effective in a variety of foods, especially at the refrigerated storage and handling temperatures typical of foods at risk for listerial contamination. The extent of food borne infections and intoxications in the United States was quantitatively documented in the CAST report of 1994 (Foodborne Pathogens: Risks and Consequences. Task Force Report No. 122, Council for Agricultural Science and Technology, Washington D.C.), as well as being extensively characterized in the past few years due to better reporting systems and programs (CDC. 1988c. 1997 Final FoodNet Surveillance report. U.S. Department of Health and Human Services, October, 1998). In order to reduce the prevalence of listeriosis and other food borne infections, a wide variety of research has been conducted to develop compositions which function as food grade anti-bacterial ingredients. Individual compounds have been disclosed in this research, with little if any commercial benefit or use, primarily because single compounds typically lack the efficacy or are too costly to use in food processing and formulations. At this time, there is still a need for better control of gram positive pathogens such as Listeria monocytogenes, Staphylococcus aureus, Bacillus cereus, Clostridium botulinum, C. perfringens, and the like, which pose significant health risks to consumers. In addition, other gram positive spoilage bacteria such as lactobacilli, streptococci, bacilli, enterococci, and micrococci species are known to cause spoilage, though not normally illness, and are often the principal agents in reducing the shelf life and freshness of selected foods. Both pathogenic and spoilage bacteria can occur in raw food materials, but heat processing tends to reduce bacterial loads dramatically. After processing, most foods are at risk for recontamination prior to packaging, distribution, and final consumption, when they may be exposed to pathogens in the food handling environment. Even in the cleanest processing facilities, selected pathogens may contaminate the already processed foods, usually at very low levels. In the case of cold tolerant pathogens, primarily various listerial species, they may then grow unchecked on the food during distribution and storage until final consumption. The more such pathogens grow in a food product, the higher the risk of infection among consumers of that food product. This is a special concern for ready to eat meats and dairy products, as such foods are not heated or processed again by the user prior to consumption. In such cases, the most likely risk is from Listeria species that grow well under refrigeration. Consumption of elevated levels of any pathogen is recognized to increase the risk of infection, especially among infants, the elderly, pregnant women, and any immune compromised individuals.

Web site: http://www.delphion.com/details?pn=US06620446__

- **Antibiotics and methods of using the same**

  Inventor(s): Novak; Rodger (New York, NY), Tuomanen; Elaine I. (Germantown, TN)

  Assignee(s): St. Jude Children's Research Hospital (Memphis, TN)

  Patent Number: 6,630,583

  Date filed: January 28, 2000

  Abstract: The present invention discloses novel **antibiotic** peptides, including naturally occurring peptides. The present invention also includes the nucleic acid sequences encoding such peptides and the corresponding amino acid sequences. Methods of identifying, making, and using the **antibiotic** peptides are also disclosed. The present invention further provides novel proteins involved in the regulation of bacterial autolysis.

  Excerpt(s): The invention relates to the field of novel **antibiotic** peptides, including naturally occurring peptides. The nucleic acid sequence encoding the peptide and the corresponding amino acid sequence are included, together with methods of using the same. Classical penicillin-type **antibiotics** bind to cell wall synthetic enzymes and thereby deregulate the activity of a single class of proteins known as autolysins which leads to bacterial lysis and bacterial cell death. The development of new drugs which affect an alternative bacterial target protein would be desirable. Pneumococcus is a particularly relevant organism for such study because 1) it has only one predominant autolysin (LytA rather than the multiple autolysins of other bacteria), 2) the autolysin has been cloned and sequenced and can therefore be easily manipulated genetically, and 3) pneumococcus has only one growth zone so that is possible to study activation of the enzyme in a fairly defined region of the cell. Most bacteria are stabilized by a cell wall consisting of a glycopeptide polymeric murein (peptidoglycan) that completely encloses the cell [Weidel & Pelzer et al., Enzymol., 26:193-232 (1964)]. Expansion of the cell wall during bacterial growth and splitting of the septum for cell separation requires enzymes that can cleave this covalently closed network. In addition to acting as spacemaker enzymes for cell wall growth [Tomasz et al., Walter de Gruyter, 155-172 (1983)], certain murein hydrolases also act as autolysins, putative suicide enzymes. The life and death dichotomy of autolysin function demonstrates the need for efficient and strict regulation of murein hydrolase activity, a paradigm conceptually similar to that for caspases in the process of eukaryotic apoptosis. Not surprisingly, the regulation of the autolysins is a highly sophisticated physiological task. For example, the enzymes must be controlled at their extracytoplasmic location. In addition, most bacteria possess multiple hydrolases which must be controlled in concert. **Antibiotics** such as penicillin induce bacteriolysis by interfering with the control of the endogenous autolytic enzymes, indicating the significant chemotherapeutic relevance of these enzymes.

  Web site: http://www.delphion.com/details?pn=US06630583__

- **Antibiotics from microbispora**

  Inventor(s): Lee; May D. (Los Altos, CA)

  Assignee(s): Essential Therapeutics, Inc. (Mountain View, CA)

  Patent Number: 6,551,591

  Date filed: September 7, 2001

Abstract: The present invention provides a novel strain of Microbispora corallina, means for identifying it, methods for culturing it at several different levels, two new **antibiotics** derived from the cultures and the physico-chemical characteristics of those compounds and their biological activity against a variety of microorganisms.

Excerpt(s): This invention relates to the fields of chemistry, bacteriology, biology, biochemistry, pharmacology and medicine. In particular it relates to two new **antibiotics** isolated from a fermentation broth of a novel strain of Microbispora corallina. Over the past 60 years, a broad range of **antibiotics,** have become available for the treatment and prevention of bacterially transmitted disease. Penicillin, streptomycin, aureomycin, cephalosporin, bacitracin, erythromycin, novobiocin, methicillin, neomycin, chloramphenicol, kanamycin, chlortetracycline,to name a few--each of these drugs, isolated from microorganisms, has provided a great benefit to the well-being of people and animals the world around. Unfortunately, the widespread use of **antibiotics,** combined with the natural proclivity of target organisms to find a way to survive such attack, has resulted in an alarming increase in the number of resistant bacterial strains. This roster of resistant species includes a number of clinically important bacteria such as Staphylococcus, Salmonella, Enterobacteriaceae and Pseudomonas, in particular, the species S. aureus and S. pneumoniae. Thus, there continues to be an urgent need for new drugs, exhibiting novel modes of action unrecognized by target organisms, to overcome the resistance of these and other species of bacteria. While a great deal of effort is being expended to design new, partially or entirely synthetic drugs to fill the voids in therapeutic efficacy created by the emergence of resistance, nature continues to be a invaluable source of such compounds.

Web site: http://www.delphion.com/details?pn=US06551591__

- **Antibiotics GE 23077, pharmaceutically acceptable salts and compositions, and use thereof**

  Inventor(s): Ciciliato; Ismaela (Busto Arsizio, IT), Corti; Emiliana (Rovellasca, IT), Kurz; Michael (Hofheim, DE), Marinelli; Flavia (Milan, IT), Montanini; Nicoletta (Malnate, IT), Sarubbi; Edoardo Giacomo (Fontenay-Sous-Bois, FR), Selva; Enrico (Gropello Cairoli, IT), Stefanelli; Stefania (Legnano, IT)

  Assignee(s): Biosearch Italia S.p.A. (Milan, IT)

  Patent Number: 6,586,393

  Date filed: November 9, 2001

  Abstract: The invention relates to an **antibiotic** substance of microbial origin, arbitrarily denominated GE23077 complex and the individual factors which constitute it, a mixture of said factors in any proportion, the pharmaceutically acceptable salts and compositions thereof, and their use as an antibacterial agent having a selective inhibitory activity against E. coli RNA polymerase.

  Excerpt(s): The present invention concerns an **antibiotic** substance of microbial origin, arbitrarily denominated GE23077 complex and the individual factors that constitute it, namely GE23077 factor A1, GE23077 factor A2, GE23077 factor B1 and GE23077 factor B2, a mixture of said factors in any proportion, the pharmaceutically acceptable salts and compositions thereof, and their use as an antibacterial agent with a selective inhibitory activity against E. coli RNA polymerase. Another object of the present invention is a process for preparing GE23077 complex, namely GE23077 factor A1, GE23077 factor A2, GE23077 factor B1 and GE23077 factor B2, a mixture of said factors

in any proportion, hereinafter reported as GE23077 compounds. Actinomadura sp. DSMZ 13491 was isolated from a soil sample and deposited on May 22, 2000, with the DSMZ, (Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Mascheroder Weg 1b, D-38124 Braunschweig, Germany), under the provision of the Budapest Treaty. The strain was accorded accession number DSMZ 13491.

Web site: http://www.delphion.com/details?pn=US06586393__

- **Anti-infection formulation and delivery method**

  Inventor(s): Dent, Jr.; James L (R.R. 1 Box 191A, Lincoln Hwy., Thomasville, PA 17364)

  Assignee(s): none reported

  Patent Number: 6,558,618

  Date filed: April 27, 1999

  Abstract: A method of dispersing, in water vapor, an anti-infective therapeutic composition (10) into the air in a room (36), in order to treat or prevent transmission of upper respiratory infections, includes: adding to a reservoir of liquid water in a vaporizer (34), a therapeutic composition (10) containing one or more **antibiotics** (14), alcohol (16), an analgesic (18) and an expectorant (20); and vaporizing the therapeutic composition (10) into the air along with the water in the vaporizer reservoir for inhalation by persons in the room.

  Excerpt(s): The instant invention relates generally to compositions for alleviating the symptoms of upper respiratory infections in humans and more specifically to anti-infection formulations for vaporizing into the air for delivery via inhalation. The present invention is concerned with an anti-infection composition for alleviating the symptoms of upper respiratory infections in humans and more specifically to anti-infection formulations for vaporizing into the, air for delivery to a person in need of such treatment via inhalation. A primary object of the present invention is to provide a therapeutic composition for addition to the water of a vaporizer for inhalation by a person in need of treating or preventing transmission of an upper respiratory tract infection (URTI).

  Web site: http://www.delphion.com/details?pn=US06558618__

- **Catechin multimers as therapeutic drug delivery agents**

  Inventor(s): Larson; Drake (P.O. Box 355, Thermal, CA 92274)

  Assignee(s): none reported

  Patent Number: 6,562,864

  Date filed: May 3, 2002

  Abstract: Described herein are catechin multimers, and particularly substituted catechin multimers, and their use as carrier moieties for the delivery of nucleophilic and cationic bioactive therapeutic agents to target sites in vivo. For example, substituted catechin multimers of the present invention may be administered alone, for the treatment of stenotic vascular diseases and disorders, such as atherosclerosis (also known as arteriosclerosis) and coronary heart disease (also known as coronary artery disease and ischemic heart disease). Alternatively, catechin multimers, substituted and otherwise, may be complexed with nucleophilic and/or cationic bioactive therapeutic agents, such

as anti-thrombotic agents, cholesterol lowering agents, anti-plaque agents, anti-cancer agents, chemotherapeutic agents, anti-inflammatory agents, **antibiotics,** antimicrobials, wound healing agents, and the like, for the treatment of a variety of diseases and disorders, including but not limited to cardiac and vascular stenoses, cancer, inflammatory conditions, neurological conditions, infection, wounds, burns and the like. The catechin multimers, particularly the substituted catechin multimers, described herein have a strong affinity for polar proteins residing in the vascular endothelium as well as cell walls and membranes, and, accordingly, are able to provide targeted delivery of bioactive agents embedded therein and/or complexed therewith so as to potentiate their therapeutic effects. The therapeutic complexes may be pharmaceutically formulated "neat" (e.g., without additives) or with additives such as pharmaceutical carriers, diluents, buffers, adjuvants, excipients, surfactants, and stabilizers.

Excerpt(s): The present invention is related to catechin multimers and their use as carrier moieties for the delivery of nucleophilic and/or cationic bioactive therapeutic agents to target sites in vivo. For example, substituted catechin multimers of the present invention may be administered alone, for the treatment of stenotic vascular diseases and disorders, such as atherosclerosis (also known as arteriosclerosis) and coronary heart disease (also known as coronary artery disease and ischemic heart disease). Alternatively, catechin multimers, substituted and otherwise, may be complexed with nucleophilic and/or cationic bioactive therapeutic agents, such as anti-thrombotic agents, cholesterol lowering agents, anti-plaque agents, anti-cancer agents, chemotherapeutic agents, anti-inflammatory agents, **antibiotics,** antimicrobials, wound healing agents, and the like, for the treatment of a variety of diseases and disorders, including but not limited to, vascular and cardiac stenoses, cancer, inflammatory conditions, neurological conditions, infections, burns, wounds, etc. Catechin multimers, particularly the substituted catechin multimers described herein, have a strong affinity for polar proteins residing in the vascular endothelium as well as the walls and membranes of other select cells and tissues, and, accordingly, are able to provide targeted delivery of bioactive agents embedded therein and/or complexed therewith so as to potentiate their therapeutic effects. Many diseases or disorders are characterized by localized pathology, i.e., affecting only select cells, tissues or organs. Examples of such diseases or disorders include but are not limited to cancers, stenotic vascular disorders such as atherosclerosis (or arteriosclerosis), inflammatory disorders, infections, wounds, burns, and certain neurological conditions. Treatment modalities for such diseases often rely on the ability to target bioactive agents to a diseased region or tissue in the body of a patient, while minimizing or preventing action of the bioactive agents on other regions or tissues in the body, such as undiseased regions or tissues. In other words, in treating such conditions, it is desirable to direct the appropriate drug to the affected area while at the same time avoiding unacceptable or toxic side effects to healthy tissue. Targeted drug delivery means are particularly important where the toxicity of the drug is an issue. Specific tissue targeting drug delivery methods potentially serve to minimize toxic side effects, lower the required dosage amounts, and decrease costs for the patient. Various methods for targeted delivery of bioactive agents are described in the literature. For example, one method involves the use of liposomes as delivery vehicles. Alternatively, structural features, such as receptor proteins and cell-specific antigens, have also been used in targeting delivery of a bioactive agent to a particular region or tissue. However, such structural features are associated with one or, at most a few, disease states. In addition, incomplete or irregular expression of such structural features may further limit their usefulness in targeted delivery of bioactive agents. Moreover, delivery of effective doses of bioactive agents to target cells is hampered by many factors, including but not limited to, low residence times in serum, ineffective targeting,

loss of the therapeutic agent in solution before it may be taken up by the target cell, and degradation of the therapeutic in the endosomic/lysosomic pathway.

Web site: http://www.delphion.com/details?pn=US06562864__

- **CBI analogs of CC-1065 and the duocarmycins**

  Inventor(s): Boger; Dale L. (La Jolla, CA)

  Assignee(s): The Scripps Research Institute (La Jolla, CA)

  Patent Number: 6,548,530

  Date filed: October 2, 1998

  Abstract: Analogs of the antitumor **antibiotics** CC-1065 and the duocarmycins incorporate the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit. The CBI-based analogs have potent cytotoxic activity and are useful as efficacious antitumor compounds. A direct relationship between functional stability and in vitro cytotoxic potency is disclosed. The CBI-based analogs are easily synthesized and are 4.times. more stable and 4.times. more potent than the corresponding analogs containing the authentic CPI alkylation subunit of CC-1065 and comparable in potency to agents containing the authentic alkylation subunit of duocarmycin SA. Similarly, the CBI-based agents alkylate DNA with an unaltered sequence selectivity at an enhanced rate and with a greater efficiency than the corresponding CPI analog and were comparable to the corresponding analog incorporating the duocarmycin SA alkylation subunit. Systematic and extensive modifications and simplifications in the DNA binding subunits attached to CBI are also described.

  Excerpt(s): The invention relates to antitumor **antibiotics.** More particularly, the invention relates to analogs of CC-1065 and the duocarmycins having antitumor **antibiotic** activity. Concurrent with the above structure/function studies, substantial efforts have been devoted to developing potential clinical candidates based on the natural product structures having enhanced in vivo efficacy. Compounds 4-8 are analogs of the natural product structures having enhanced in vivo efficacy with clinical potential. (D. L. Boger, et al., J. Org. Chem. 1984, 49, 2240; M. A. Warephoski, M. A. Tetrahedron Lett. 1986, 27, 4103; Li, L. H.; Invest New Drugs 1991, 9, 137; B. K. Bhuyan, et al., Cancer Res. 1992, 52, 5687; B. K. Bhuyan, et al., Cancer Res. 1993, 53, 1354; L. H. Li, et al., Cancer Res. 1992, 52, 4904; M. A. Mitchell, et al., J. Am. Chem. Soc. 1991, 113, 8994. Lee, C.-S.; Gibson, N. W. Cancer Res. 1991, 51, 6586. Lee, C.-S.; Gibson, N. W. Biochemistry 1993, 32, 9108; Wierenga, W. Drugs Fut. 1991, 16, 741; K. Gomi, et al., Jpn. J. Cancer Res. 1992, 83, 113. Okamoto, A.; Okabe, M.; Gomi, K. Jpn. J. Cancer Res. 1993, 84, 93; E. Kobayashi, et al., Cancer Res. 1994, 54, 2404; and H. Ogasawara, Jpn. J. Cancer Res. 1994, 85, 418. ) A Phase I clinical trial one one drug candidate in this class is described by G. F. Fleming, et al., (J. Natl. Cancer Inst. 1994, 86, 368.) Efforts have also focused on the development of analogs having decreased delayed toxicity as compared to the natural form of (+)-CC-1065. (J. P. McGovren, et al., Cancer Res. 1993, 53, 5690.) Importantly, this unusual property has not been observed with ent-(-)-CC-1065, although it is equally cytotoxic, and is not observed with the naturally-derived duocarmycins as well as simplified analogs of the natural products. The first preparation and examination of agents containing the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit were described in connection with efforts to evaluate CC-1065 and duocarmycin analogs bearing deep-seated structural alterations in the alkylation subunit. (D. L. Boger, et al., J. Am. Chem. Soc. 1989, 111, 6461; and D. L. Boger, et al., J. Org. Chem. 1990, 55, 5823.) These agents

were employed as tools to identify the structural features of compounds 1-3 associated with their sequence selective alkylation of duplex DNA and to define the fundamental relationships between structure, chemical or functional reactivity and biological properties.

Web site: http://www.delphion.com/details?pn=US06548530__

- **Circumcision/penile dressing**

  Inventor(s): Jennings-Spring; Barbara (10844 N. Dogwood Trail, Jupiter, FL 33478)

  Assignee(s): none reported

  Patent Number: 6,580,011

  Date filed: July 24, 2000

  Abstract: A dressing for a penis includes a sleeve bandage portion with outwardly extending securement straps. Fastening material can be affixed to the distal ends of the securement straps. The sleeve bandage portion can be configured to be placed on the circumcised penis so as to sheath the penis. After the sleeve bandage is placed on the penis, the dressing can be secured in place by diametrically wrapping the securement straps around the sleeve bandage by engaging the fastening material on the securement straps to the surface of the sleeve bandage. The bandage can be packaged in a hygienically sealed foil package openable at a top edge which allows the bandage to be removed with a minimal amount of handling. Topical **antibiotics** and anesthetics, as well as petroleum jelly, can be incorporated into the sleeve bandage.

  Excerpt(s): This invention relates to post-operative wound dressings, and in particular to wound dressings to be applied to a penis. Circumcision is one of the oldest of all surgical procedures, and is the operation most frequently performed on males in the United States. While circumcision is sometimes performed on adults and young children, the operation is most commonly performed on newborn infants. As in any surgical procedure, there is a risk of infection associated with circumcision. Cleanliness and proper dressing of the wound site is of utmost importance. Bandages applied to the penile area are difficult to maintain, and the application of post-surgical dressings to infants presents particular problems. Ordinary strip gauze material and 4".times.4" gauze is frequently used to bandage the newly circumcised penis of an infant. The necessity of simultaneously diapering the infant tends to interfere with the placement of the bandage, as the removal of the diaper may rip away the bandage. The delicacy of the operated area, as well as the need for frequent changing of the dressing, preclude the use of strenuous means to secure the bandage, such as excessive taping and pressing to mold gauze material to the newly circumcised penis. The application of ordinary bandaging materials to the penis of an infant can therefore be awkward, and such a bandage can easily fall off, leaving the infant susceptible to infection.

  Web site: http://www.delphion.com/details?pn=US06580011__

- **Compositions including antibiotics and methods for using same**

  Inventor(s): Bancroft; Elizabeth A. (Irvine, CA), Cheetham; Janet K. (Laguna Niguel, CA), Jensen; Harold G. (Lake Forest, CA), Kuan; Teresa H. (Placentia, CA), Muller; Christopher A. (Foothill Ranch, CA), Power; David F. (Trabuco Canyon, CA), Skule; Kevin D. (Rancho Santa Margarita, CA)

  Assignee(s): Allergan, Inc. (Irvine, CA)

  Patent Number: 6,552,020

  Date filed: July 24, 2000

  Abstract: Compositions including a quinolone component, such as ofloxacin, having fungistatic activity in the compositions, present in an amount effective as an **antibiotic** when the composition is placed in a mammalian eye, a NSAID component present in an amount to reduce inflammation or pain when the composition is placed in the eye, and a carrier component in an amount effective to act as a carrier for the quinolone component and NSAID component are provided. Methods of using the present compositions, for example, to resolve microbial infections and/or to reduce inflammation and/or pain in a mammalian eye are included within the scope of the present invention. Methods for treating corneal injuries are also included. In addition, methods for treating ocular infections, for example, corneal infections, are included.

  Excerpt(s): The present invention relates to compositions including **antibiotics** and to methods for using such compositions. More particularly, the invention relates to compositions including **antibiotics** which have added protection against fungal contamination, which reduce inflammation or pain and/or which are useful in the treatment of corneal ulcers. Various **antibiotic** components have been used in ocular applications, for example, to control or manage or prevent ocular infections and the like. Moreover, **antibiotic** components, such as tobramycin have been suggested for use in combination with other materials, such as ophthalmically acceptable non-steroidal anti-inflammatory drugs or NSAIDs. See, for example, Fu et al. U.S. Pat. No. 5,414,011, the disclosure of which is incorporated in its entirety herein by reference. Quinolones, such as ofloxacin, have been used in compositions for treating ocular infections. These **antibiotic** compositions include one or more additional components which act as preservatives, for example, benzalkonium chloride (BAK) or organomercurials. Antibiotic compositions, even with preservatives, have been susceptible to microbial, for example, fungal, contamination. In addition, preservatives tend to cause irritation, allergic reactions, and/or other detrimental side effects when the preserved composition is administered to a patient.

  Web site: http://www.delphion.com/details?pn=US06552020__

- **Device for isolation and surface culture of microorganisms from bulk fluids**

  Inventor(s): Hyman; Jones M. (Durham, NC), Jeffrey; Scott R. (Raleigh, NC), Maresch; Martin J. (Willmar, MN), Matsumura; Paul M. (Cary, NC), Thorpe; Thurman C. (Durham, NC)

  Assignee(s): bioMerieux, Inc. (Durham, NC)

  Patent Number: 6,596,532

  Date filed: February 11, 2000

Abstract: A device and method are provided for isolating and culturing microorganisms from a bulk fluid sample. The device comprises a container having therein a polymeric immobilization layer having interstitial spaces between polymer chains such as a gel matrix. The interstitial spaces are of an average size less than an average size of microorganisms to be separated from the sample and cultured. A bulk fluid sample is applied to the immobilization layer where fluid is absorbed by the layer and microorganisms remain on the surface of the layer. After culturing, microorganism colonies are readily accessible on the surface of the layer for harvest and testing. The immobilization layer may contain one or more of nutrients for microorganism growth, lytic agents, lytic enzymes, **antibiotics, antibiotic** neutralizers, indicators, detergents and selective agents. An adjacent support layer may be above and/or below the immobilization layer. The immobilization layer may be in combination with a sensor layer that changes color in areas corresponding to portions of the layer having microorganisms thereon. A membrane may be embedded in the immobilization layer for enhancing microorganism visibility and facilitating microorganism harvest.

Excerpt(s): This application is related to U.S. patent application Ser. No. 08/989,560 to Jeffrey et al. filed Dec. 12, 1997, and U.S. patent application Ser. No. 09/113,929 to Maresch et al. (now U.S. Pat. No. 5,912,115), the subject matter of each being incorporated herein by reference. The presence of microbial contamination in clinical specimens is conventionally determined by culturing the specimens in the presence of nutrients and detecting microbial activity through changes in the specimen or in the atmosphere over the specimen after a period of time. For example, in the U.S. Pat. No. 4,182,656 to Ahnell et al., the sample is placed in a container with a culture medium comprising a carbon 13 labeled fermentable substrate. After sealing the container and subjecting the specimen to conditions conducive to biological activity, the ratio of carbon 13 to carbon 12 in the gaseous atmosphere over the specimen is determined and compared with the initial ratio. In U.S. Pat. No. 4,152,213, a method is claimed by which the presence of oxygen consuming bacteria in a specimen is determined in a sealed container by detecting a reduction in the amount of oxygen in the atmosphere over the specimen through monitoring the pressure of gas in the container. U.S. Pat. No. 4,073,691 provides a method for determining the presence of biologically active agents, including bacteria, in a sealed container containing a culture medium by measuring changes in the character of the gaseous atmosphere over the specimen after a period of time. A method for non-invasive detection is taught by Calandra et al., U.S. Pat. No. 5,094,955, where a device is disclosed for detecting the presence of microorganisms in clinical specimens, such as blood or other body fluids, and in non-clinical specimens, by culturing the specimens with a sterile liquid growth medium in a transparent sealed container. The presence of microorganisms is determined by detecting or measuring changes in the pH of the specimen or the production of carbon dioxide within the specimen using a sensor affixed to the interior surface of the container or to the sealing means used to seal the container. In Calandra et al., microorganisms can be detected in the presence of interfering material, such as large concentrations of red blood cells, through non-radiometric and non-invasive means.

Web site: http://www.delphion.com/details?pn=US06596532__

- **Exonuclease-mediated nucleic acid reassembly in directed evolution**

  Inventor(s): Short; Jay M. (Rancho Santa Fe, CA)

  Assignee(s): Diversa Corporation (San Diego, CA)

  Patent Number: 6,635,449

  Date filed: March 26, 2002

  Abstract: This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of exonuclease-mediated reassembly methods is the ability to reassemble nucleic acid strands that would otherwise be problematic to chimerize. Exonuclease-mediated reassembly methods can be used in combination with other mutagenesis methods provided herein. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of **antibiotics,** pharmacotherapeutics, and transgenic traits.

  Excerpt(s): This invention relates to the field of protein engineering. More specifically, this relates to a directed evolution method for preparing a polynucleotides encoding polypeptide, which method comprises the step of generating site-directed mutagenesis optionally in combination with the step of polynucleotide chimerization, the step of selecting for potentially desirable progeny molecules, including by a process termed end-selection (which may then be screened further), and the step of screening the polynucleotides for the production of polypeptide(s) having a useful property. In a particular aspect, the present invention is relevant to enzymes, particularly to thermostable enzymes, and to their generation by directed evolution. More particularly, the present invention relates to thermostable enzymes which are stable at high temperature and which have improved activity at lower temperatures. Harvesting the full potential of nature's diversity can include both the step of discovery and the step of optimizing what is discovered. For example, the step of discovery allows one to mine biological molecules that have industrial utility. However, for certain industrial needs, it is advantageous to further modify these enzymes experimentally to achieve properties beyond what natural evolution has provided and is likely to provide in the near future.

  Web site: http://www.delphion.com/details?pn=US06635449__

- **Expression system for producing proteins**

  Inventor(s): Hessing; Johanna (Delft, NL), Pfaller; Rupert (Munchen, DE), van den Hondel; Cornelis (Gouda, NL), van Gorcom; Robertus (Soest, NL)

  Assignee(s): Consortium fur Electrochemische Industrie GmbH (Munchen, DE)

  Patent Number: 6,551,797

  Date filed: February 28, 2001

  Abstract: An expression system for producing a protein in a filamentous fungus, consisting of a) a host organism selected from the species Trametes and Polyporus and b) a DNS vector containing a selection marker gene. This selection marker gene code is a protein which allows the selection of positive transformants after the transformation of the host organism and which is selected from the group of: antibiotics-resistant genes coding for proteins which eliminate the growth-inhibitory effect of **antibiotics** against which the host organism is not resistant. Genes coding proteins which are capable of a color-causing reaction; and genes complementing a genetic defect of the host organism (auxotrophy), the expression of the selection marker gene is controlled by at least one active genetic regulation element in the host organism, and c) a DNS vector containing a gene which codes the protein to be produced. The expression of this gene and optionally, the secretion of the protein so produced are controlled by an active genetic regulation element in the host organism. The DNS vector containing a section marker gene and the DNS vector containing the gene which codes the protein to be produced can also be in the form of one DNS vector.

  Excerpt(s): The invention relates to an expression system for production of proteins in fungi of the genera Trametes or Polyporus, to its preparation and to its use. Various prokaryotic and eukaryotic expression systems are known for protein production. Examples of prokaryotic expression systems are Escherichia coli and Bacillus subtilis. The methods for genetic manipulation of these organisms are well established. Specific disadvantages of these expression systems are the frequently disappointingly low production rate in particular of eukaryotic proteins, the folding of the produced proteins in such a way that they are often not in active form, and, in particular, the absence of the post-translational modification of the expressed proteins. As example of the absence of post-translational modification, mention may be made of the absence of incorporation of prosthetic groups or the absence of glycosylation of the protein to be expressed. These disadvantages of prokaryotic expression systems can be avoided by using eukaryotic systems.

  Web site: http://www.delphion.com/details?pn=US06551797__

- **Gamma-hydroxy-2-(fluoroalkylaminocarbonyl)-1-piperazinepentanamides and uses thereof**

  Inventor(s): Armstrong, III; Joseph D. (Westfield, NJ), Askin; David (Warren, NJ), Chapman; Kevin T. (Scotch Plains, NJ), Cheng; Yuan (Edison, NJ), Duffy; Joseph Leslie (Cranford, NJ), Fleitz; Fred J. (Franklin Park, NJ), Hoerrner; R. Scott (Westfield, NJ), Huening; Tracy (Madison, NJ), Kevin; Nancy J. (East Brunswick, NJ), Kirk; Brian Anthony (Basking Ridge, NJ), Lu; Zhijian (Clinton, NJ), Petrillo; Daniel E. (Hoboken, NJ), Purick; Robert (Edison, NJ), Raghavan; Subharekha (Teaneck, NJ), Rano; Thomas A. (Somerville, NJ), Tata; James R. (Westfield, NJ), Varsolona; Richard J. (Scotch Plains, NJ), Zhang; Fengqi (Edison, NJ)

  Assignee(s): Merck & Co., Inc. (Rahway, NJ)

  Patent Number: 6,642,237

  Date filed: November 21, 2000

  Abstract:.gamma.-Hydroxy-2-(fluoroalkylaminocarbonyl)-1-piperazinepentanamide compounds are inhibitors of HIV protease and inhibitors of HIV replication. These compounds are useful in the prevention or treatment of infection by HV and the treatment of AIDS, either as compounds, pharmaceutically acceptable salts, pharmaceutical composition ingredients, whether or not in combination with other antivirals, immunomodulators, **antibiotics** or vaccines. Methods of treating AIDS and methods of preventing or treating infection by HIV are also described. These compounds are effective against HIV viral mutants which are resistant to HIV protease inhibitors currently used for treating AIDS and HIV infection.

  Excerpt(s): The present invention is directed to.gamma.-hydroxy-2-(fluoroalkylaminocarbonyl)-1-piperazinepentanamide compounds, their pharmaceutically acceptable salts, their synthesis, and their use as inhibitors of HIV protease. The compounds of the present invention are useful for preventing or treating infection by HIV and for treating AIDS. References are made throughout this application to various publications in order to more fully describe the state of the art to which this invention pertains. The disclosures of these references are hereby incorporated by reference in their entireties for all purposes. A retrovirus designated human immunodeficiency virus (HIV) is the etiological agent of the complex disease that includes progressive destruction of the immune system (acquired immune deficiency syndrome; AIDS) and degeneration of the central and peripheral nervous system. This virus was previously known as LAV, HTLV-III, or ARV. A common feature of retrovirus replication is the extensive post-translational processing of precursor polyproteins by a virally encoded protease to generate mature viral proteins required for virus assembly and function. Inhibition of this processing prevents the production of normally infectious virus. For example, Kohl et al., Proc. Nat'l Acad. Sci. 1988, 85: 4686, demonstrated that genetic inactivation of the HIV encoded protease resulted in the production of immature, non-infectious virus particles. These results indicated that inhibition of the HIV protease represents a viable method for the treatment of AIDS and the prevention or treatment of infection by HIV.

  Web site: http://www.delphion.com/details?pn=US06642237__

- **Immobilizing mediator molecules via anchor molecules on metallic implant materials containing oxide layer**

  Inventor(s): Jennissen; Herbert Peter (Essen, DE)

  Assignee(s): Morphoplant GmbH (Bochum, DE)

  Patent Number: 6,635,269

  Date filed: May 23, 2000

  Abstract: A mediator molecule is immobilized on the surface of a metallic or ceramic implant material. An anchor molecule such as a dialdehyde having a functional group that covalently binds the mediator molecule is covalently bound to the surface, and the mediator molecule is coupled to the functional group of the anchor molecule. The implant material may be composed of titanium, titanium alloy, aluminum, stainless steel or hydroxylapatite. Oxide units on the surface of the implant material can be increased preferably by treating with hot chromic-sulphuric acid for 0.5 to 3 hours at a temperature between 100 to 250.degree. C. prior to binding the anchor molecule. Also, prior to binding the anchor molecule, the surface of the implant material can be activated by reacting with a silane derivative. Mediator molecules include BMP protein, ubiquitin and **antibiotics,** and the implant material may be an artificial joint or coronary vessel support such as a stent.

  Excerpt(s): The present invention relates to a method for the immobilization of mediator molecules on surfaces of metallic or ceramic materials which are used for implants such as artificial joints or also microimplants, for example so-called stents, as well as implants produced according to the method. The implantation of artificial joints or bones has gained increasing importance in recent years, for example in the treatment of joint dysplasias or joint dislocations or in sicknesses resulting from joint attrition as a result of improper joint positioning. The function of the implants and the materials used for their production, which, in addition to metals such as titanium or metal alloys, can also include ceramics or synthetic materials such as teflon, have been continually improved, so that following a successful healing process, implants exhibit lifetimes of 10 years in 90-95% of all cases. Yet despite this progress and these improved operational methods, an implantation still remains a difficult and strenuous operation, particularly since it is associated with a long process of healing-in of the implants, often including month-long stays in clinics and health resorts, including rehabilitation measures. In addition to the pain, the length of the treatment period and the separation from familiar surroundings represent heavy stresses for the affected patients. In addition, the long healing process incurs high personal and treatment costs due to the required intensive care. The understanding of the molecular-lever processes required for a successful growing-in of an implant has markedly increased in recent years. Structural compatibility and surface compatibility are crucial for the tissue tolerability of an implant. Biocompatibility in a narrower sense depends only on the surface. Proteins play a crucial role at all levels of integration. These form an initially adsorbed protein layer as early as during the implantation operation and thus, as explained below, since the first cells will later colonize on this layer, determine the further progression of the healing-in of the implant.

  Web site: http://www.delphion.com/details?pn=US06635269__

- **Isolated nucleic acids from Micromonospora rosaria plasmid pMR2 and vectors made therefrom**

  Inventor(s): Horan; Ann C. (Summit, NJ), Hosted, Jr.; Thomas J. (Summit, NJ)

  Assignee(s): Schering Corporation (Kenilworth, NJ)

  Patent Number: 6,569,668

  Date filed: March 29, 2001

  Abstract: Plasmid genes from Micromonospora rosaria pMR2 have been isolated, cloned, sequenced and functionally identified. These genes have been used to create vectors which can be used to express actinomycete genes, manipulate metabolic pathways and produce useful gene products such as hybrid **antibiotics.**

  Excerpt(s): The present invention relates generally to isolated nucleic acids and the creation of vectors incorporating the same for the study and expression of genes in actinomycetes. The invention more particularly relates to novel genes isolated from a Micromonospora plasmid which can be used in the construction of vectors for the study and expression of genes and manipulation of metabolic pathways in actinomycete hosts. Actinomycetes are branched filamentous Gram-positive bacteria. Streptomyces, Micromonospora, Nocardia, Actinoplanes, Saccharopolyspora, Actinomadura, Thermomonospora, Microbispora, Streptosporangium and others all represent genera of the Actinomycetes (Atlas of Actinomycetes, Asakura Publishing Co., Ltd 1996). Actinomycetes are very important industrially because they produce a variety of secondary metabolites such as **antibiotics,** herbicides, anticancer agents, antihelmintics, and anabolic agents (Demain., Appl. Microbiol and Biotechnology., 1999, 52:455-463). **Antibiotics** are a large and complex group of chemical substances which exert deleterious effects on other organisms, many of which organisms are harmful to humans. Thus, **antibiotics** are particularly important secondary metabolites to study and produce. This is especially true because many pathogens can develop **antibiotic** resistance to known **antibiotics.** Given the actinomycetes' proclivity for producing secondary metabolites such as **antibiotics,** it is especially advantageous to develop new tools such as vectors, promoters and the like to allow actinomycetes to be easily genetically manipulated. These tools would make it possible to control the levels of expression of genes encoding for secondary metabolites and also would make it possible to prepare derivatives or intermediates of these metabolites. In addition, the development of new vectors utilizing novel genes would make it possible to program microorganisms such as actinomycetes to produce recombinant products such as hybrid **antibiotics** via genetic engineering techniques.

  Web site: http://www.delphion.com/details?pn=US06569668__

- **Lactic ferment comprising a particular strain of lactobacillus acidophilus and use thereof**

  Inventor(s): Luquet; Fran.cedilla.ois-Marie (Orsay, FR)

  Assignee(s): Bio-K + International Inc. (Laval, CA)

  Patent Number: 6,607,905

  Date filed: May 28, 1999

  Abstract: The purified strain of Lactobacillus acidophilus CNCM/I-1492 (L.a. 1492) when administered alone or in combination with another Lactobacillus acidophilus

(L.a.) strain and Lactobacillus casei (L.c.) strain, has a beneficial effect on the cholesterol blood level in mammals. It also strenghtens the immune system, facilitates the absorption of nutrients and stimulates the intestinal flora. Such strains also neutralize side effects caused by **antibiotics.** The invention concerns the specific strain L.a. I-1492, a ferment comprising L.a. I-1492, L.a. and L.c. strains, a dairy product obtained by this ferment and a method of manufacturing the dairy product.

Excerpt(s): The present invention concerns a purified strain Lactobacillus acidophilus identified as CNCM/I-1492 (hereinafter called L.a. I-1492), the microorganism from this strain, a lactic ferment comprising this strain, a process for making dairy products using this ferment, and the dairy products obtained by this process and containing at least 500 million per gram of Lactobacillus acidophilus (including the L.a. I-1492 strain) or 380 million/gram of L.a. I-1492. The invention also concerns the use of a ferment comprising the strain Lactobacillus acidophilus CNCM/I-1492 and of a dairy product containing the same in the pharmaceutical field for reducing the level of cholesterol in the blood of a mammal. Yogurts are fermented dairy products obtained by fermentation of different lactic bacterias with milk. The most widely used milk is cow's milk. These lactic bacterias (mainly Streptococcus thermophilus and Lactobacillus bulgaricus) are foreign bodies to the human intestinal flora and are not implanted in the digestive system during consumption of these dairy products.

Web site: http://www.delphion.com/details?pn=US06607905__

- **Method for the synthesis of pyrrole and imidazole carboxamides on a solid support**

  Inventor(s): Baird; Eldon E (Pasadena, CA), Dervan; Peter B. (San Marino, CA)

  Assignee(s): California Institute of Technology (Pasadena, CA)

  Patent Number: 6,545,162

  Date filed: July 22, 1999

  Abstract: The present invention describes a novel method for the solid phase synthesis of polyamides containing imidazole and pyrrole carboxamides. The polyamides are prepared on a solid support from aromatic carboxylic acids and aromatic amines with high stepwise coupling yields (>99%), providing milligram quantities of highly pure polyamides. The present invention also describes the synthesis of analogs of the natural products Netropsin and Distamycin A, two antiviral **antibiotics.** The present invention also describes a novel method for the solid phase synthesis of imidazole and pyrrole carboxamide polyamide-oligonucleotide conjugates. This methodology will greatly increase both the complexity and quantity of minor-groove binding polyamides and minor-groove binding polyamide-oligonucleotide conjugates which can be synthesized and tested.

  Excerpt(s): This invention relates to the field of peptide chemistry. Specifically, this invention relates to a novel process for preparing polyamides and polyamide conjugates containing imidazole and pyrrole carboxamides using solid state chemistry. Also included in this invention is a simple and effective method for preparing analogs of the antiviral **antibiotics** Netropsin and Distamycin A. Proteins and peptides play a critical role in virtually all biological processes, functioning as enzymes, hormones, antibodies, growth factors, ion carriers. **antibiotics,** toxins. and neuropeptides. Biologically active proteins and peptides. therefore, have been a major target for chemical synthesis. Chemical synthesis is used to verify structure and to study the relationship between structure and function, with the goal of designing novel compounds for potential

therapeutic use. Thus, modified or novel peptides may be synthesized which have improved therapeutic activity and/or reduced side effects. There are two basic methods for synthesizing proteins and peptides: the chemistry is either carried out in solution (solution phase) or on a solid support (solid phase). A major disadvantage of solution phase synthesis of peptides is the poor solubility of the protected peptide intermediates in organic solvents. Additionally, solution phase synthesis requires extensive experience on the part of the scientist and the purifications are difficult and time consuming. Solid phase synthesis overcomes these problems and thus, has become the method of choice in synthesizing peptides and proteins.

Web site: http://www.delphion.com/details?pn=US06545162__

- **Natural and synthetic supplements to engineered annulus and disc tissues**

  Inventor(s): Ferree; Bret A. (1238 Cliff Laine Dr., Cincinnati, OH 45208)

  Assignee(s): none reported

  Patent Number: 6,648,920

  Date filed: June 13, 2002

  Abstract: Fibrocytes, annulus fibrosis cells, cells that differentiate into annulus fibrosis cells, or cells that function like annulus fibrosis cells are harvested and combined with the extracellular matrix of the annulus fibrosis from a recently deceased human or animal to produce an engineered annulus fibrosis. Any suitable material(s) are then added to the engineered disc tissue to restore disc height. For example, a shape-memory material or alloy that changes shape from a long narrow shape to a spherical shape would facilitate insertion through a relatively small incision followed by useful height restoration. Additional therapeutic substances like culture medium, growth factors, differentiation factors, hydrogels, polymers, **antibiotics,** anti-inflammatory medications, or immunosuppressive medications could be added to the transplanted annulus fibrosis tissue. The process can be used to replace or repair other tissues or organs of the body such as the meniscus of the knee.

  Excerpt(s): This invention relates generally to the treatment of diseased or traumatized intervertebral discs, and more particularly, to the use of engineered tissues in conjunction with such treatments. Intervertebral discs provide mobility and a cushion between the vertebrae. At the center of the disc is the nucleus pulposus. The nucleus pulposus is surrounded by the annulus fibrosis, which is comprised of cells (fibrocyte-like and chondrocyte-like), collagen fibers, and non-fibrillar extracellular matrix. The components of the annulus are arranged in 15-25 lamellae around the nucleus pulposus. The fibers in the lamellae alternate their direction of orientation by 30 degrees between each band. The annulus fibrosis has three important functions. First, the annulus contains the nucleus pulposus. Second, the annulus fibrosis, with other ligaments, connects the vertebrae of the spine. Lastly, the annulus fibrosis helps to control movement between the vertebrae.

  Web site: http://www.delphion.com/details?pn=US06648920__

- **Phosphopantetheinyl transferases and uses thereof**

  Inventor(s): Gehring; Amy M. (Beulah, MI), Lambalot; Ralph H. (Wrentham, MA), Reid; Ralph (San Francisco, CA), Walsh; Christopher T. (Wellesley, MA)

  Assignee(s): President and Fellows of Harvard College (Cambridge, MA), The Regents of the University of California (Oakland, CA)

  Patent Number: 6,579,695

  Date filed: October 11, 1996

  Abstract: The invention pertains to isolated phosphopantetheinyl transferases, such as the E. coli acyl carrier protein synthase, which transfer a phosphopantetheinyl group onto a substrate. The enzyme can be purified from a natural source, produced recombinantly, or synthetically. Accordingly, the invention provides compositions and kits including phosphopantetheinyl transferases and host cells expressing phosphopantetheinyl transferases. The invention also provides nucleic acids encoding phosphopantetheinyl transferases and vectors comprising such nucleic acids. The invention further provides methods for phosphopantetheinylating a substrate in vitro or in vivo and methods for producing **antibiotics** in vitro or in vivo.

  Excerpt(s): Acyl carrier protein (ACP) is a small acidic protein (8,800 Da) responsible for acyl group activation in fatty acid biosynthesis. The gene encoding ACP (acpP) has been cloned and overexpressed (Rawlings, M. and Cronan, J. E., Jr. (1992) J. Biol. Chem., 267, 5751-5754; Jones, A. L., et al. (1993) Biochem. Soc. Trans., 21, 202S) and the solution structure of ACP has been solved by NMR spectroscopy (Holak, T. et al. (1988) Eur. J. Biochem. 175:9-15). Homologs of E. coli ACP exist throughout nature in two forms; either as an integral domain of a much larger multifunctional enzyme (type I) or as a discrete protein capable of associating with several other enzymes constituting a multienzyme synthase complex (type II). In these two forms, ACPs play central roles in a broad range of other biosynthetic pathways that depend on iterative acyl transfer steps, including polyketide (Shen, B., et al. (1992) J. Bacteriol. 174:3818-3821), non-ribosomal peptide (Baldwin, J. E., et al. (1991) J. Antibiot. 44:241-247), and depsipeptide biosynthesis (Rusnak, F., et al. (1991) Biochemistry 30:2916-2927) as well as in the transacylation of oligosaccharides (Geiger, O., et al. (1991) J. Bacteriol. 173:2872-2878) and proteins (Issartel, J. P., et al. (1991) Nature 351:759-761). A definitive feature of ACP is the 4'-phosphopantetheine (4'-PP) prosthetic group (Majerus, P. W. et al. (1965) Proc. Natl. Acad. Sci. USA 53:410-417). 4'-PP is attached through a phosphodiester linkage to a conserved serine residue found in all ACPs. Acyl groups of the many substrates recognized by type I and type II ACPs are activated for acyl transfer through a thioester linkage to the terminal cysteamine thiol of the 4'-PP moiety. The.beta.-alanyl and pantothenate portions of the 4'-PP structure are believed to serve as a tether between the phosphodiester-ACP linkage and the terminal thioester, suggesting that 4'-PP may function as a swinging arm, shuttling growing acyl chains between various active sites, e.g. as in the sequential addition of 11 amino acids by the 800 kDa cyclosporin synthetase (Lawen, A. and Zocher, R. (1990) J. Biol. Chem. 265:11355-11360). Holo-ACP synthase (holo-ACPS) transfers the 4'-PP moiety from Coenzyme A (CoA) to Ser-36 of apo-ACP to produce holo-ACP and 3',5'-ADP in a Mg.sup.2+ dependent reaction. The (acyl carrier synthase protein) ACPS from E. coli was partially purified 780-fold from crude extracts (Elovson, J. and Vagelos, P. R. (1968) J. Biol. Chem. 243:3603-3611), and the ACPS from spinach has been partially purified (Elhussein, S. A., et al. (1988) Biochem. J. 252:39-45), but remarkably little has been shown about the mechanism or specificity of this post-translational phosphopantetheinylation process. A mutant of E. coli conditionally defective in the synthesis of holo-ACP has been identified and the

mutant phenotype attributed to an altered holo-ACP synthase activity (Polacco, M. L. and Cronan, J. E., Jr. (1981) J. Biol. Chem. 256:5750-5754).

Web site: http://www.delphion.com/details?pn=US06579695__

- **Process for making optically active.alpha.-amino ketones and selected novel optically active.alpha.-amino ketones**

  Inventor(s): Talley; John J. (Chesterfield, MO)

  Assignee(s): Monsanto Company (St. Louis, MO)

  Patent Number: 6,541,654

  Date filed: October 11, 2001

  Abstract: The invention includes selected novel optically active.alpha.-amino ketones which either are themselves useful or are intermediates for the preparation of known ketomethylene pseudopeptides useful as **antibiotics, antibiotic** enhancers, or enzyme inhibitors. Further, the present invention provides a method for dehydrogenation/asymmetrical hydrogenation to obtain essentially pure antipodes of ketomethylene pseudopeptides having two chiral centers.

  Excerpt(s): The preparation of optically active alpha-amino ketones by dehydrogenation of racemic alpha-amino ketones and hydrogenation using an asymmetric hydrogenation catalyst is disclosed for dehydroketomethylene pseudopeptides having an aromatic substituent adjacent the keto group in U.S. Pat. No. 4,277,420; East German Application Nos. 280,527; 280,528; 280,529; 240,372 described in corresponding Derwent Abstract Numbers 90-362220/49, 90-362221/49, 90-362222/49, 87-057083/09, respectively. German Appl. No. 140-036 described in Derwent Abstract No. 34661C/20. Chem. Ber. 1981, 114, pp. 1137-49.

  Web site: http://www.delphion.com/details?pn=US06541654__

- **Reproductive cultures containing colloidal silver**

  Inventor(s): Simmet; Ludwig O. (Verona, WI)

  Assignee(s): Minitube of America, Inc. (Verona, WI)

  Patent Number: 6,596,472

  Date filed: June 14, 2001

  Abstract: A colloidal dispersion of nanoparticles of silver is used to preserve animal reproductive samples such as boar semen without the use of **antibiotics.** The colloidal silver solution may have a metal concentration of at least about 1.times.10-9 moles/liter and may be mixed with conventional culture media such as semen extender.

  Excerpt(s): A substantial proportion of the swine produced in North America today are produced utilizing artificial insemination. Thus, the ability to preserve animal reproductive samples, such as semen, oocytes and embryos, for use in artificial insemination and other reproductive processes is important. Without this ability, it is not possible to transport animal reproductive samples or store the samples for any length of time; thus, the utility of the samples is limited. To protect reproductive samples from bacterial contamination, it has been common practice to introduce **antibiotics** into the preservation mediums or extender solutions. Although conventional

**antibiotics** can be a low cost and effective way of preserving the samples, there are long term consequences of the continued widespread use of **antibiotics.** Over time, bacteria come to the fore which are resistant to **antibiotics.** The presence of low levels of **antibiotics** in agricultural livestock and human food products is considered to be one cause of the increasingly resistant bacteria. The increased resistance of bacteria to **antibiotics** poses a danger to humans and animals as infectious diseases are becoming more difficult to treat. Hence, in certain regions, conventional **antibiotics** are no longer effective. Moreover, there is consideration being given by regulatory bodies to banning the general use of **antibiotics** in animals raised for food production. Thus, it is desirable to have an extender that has antimicrobial properties, but is substantially free of **antibiotics.** It is also desirable to have a method for preserving animal reproductive samples that uses an extender that has antibicrobial properties, but is substantially free of **antibiotics.** The method of this invention mixes a colloidal suspension of silver as a component of a preservation medium for the preservation of animal reproductive samples. By adding the colloidal suspension of silver to conventional semen extenders, for example, an extender for boar semen which has antimicrobial properties, but substantially free of **antibiotics** is produced. A colloidal silver solution having a silver concentration of at least about 1.times.10.sup.-9 moles/liter has been found effective in preserving some reproductive materials.

Web site: http://www.delphion.com/details?pn=US06596472__

- **Shunt**

  Inventor(s): Cowan, Jr.; John A. (370 Village Green, Apt. 104, Ann Arbor, MI 48105), Murphy; Kieran (119 Beechdale Rd., Baltimore, MD 21210), Rigamonti; Daniele (2807 Old Court Rd., Baltimore, MD 21208), Williams; Michael (1394 Rivermist Ct., Baltimore, MD 21226)

  Assignee(s): none reported

  Patent Number: 6,585,677

  Date filed: August 29, 2001

  Abstract: A shunt for draining cerebral spinal fluid from the brain is provided. In an embodiment, the shunt includes a master control unit that is located in the abdomen, which interconnects a ventricular catheter and a second catheter, typically located in the peritoneal cavity. In a specific embodiment, the master control unit includes a variety of `smart` features including at least one access port to allow the injection of solutions for the prevention or removal of blockages in the catheter, and/or **antibiotics.** The access port can have other uses, such as allowing a point of access for physical navigation of a catheter or the like within the shunt, thereby providing another option for breaking-up blockages, and/or allowing an access point for repairing the shunt's components. Additionally, the master control unit includes a diagnostic unit that transmits, either wirelessly or through a wired connection via the access port, diagnostic information about the status of the patient and/or the shunt.

  Excerpt(s): The present invention relates generally to apparatuses for the treatment of hydrocephalus or the like, and more particularly relates to cerebrospinal fluid ("CSF") shunts. More particularly, ventriculoperitoneal ("VP") shunts are designed to drain CSF from the brain into the peritoneal cavity. VP shunts are used in a variety of medical conditions and are implanted in both young and old patients. Certain configurations of prior art VP shunts can include a ventricular catheter, a flow-valve that can be changed by an external magnet, and a tunneled abdominal catheter. Further discussion on this

type of shunt can be found in Reinprecht A., et al., "The Medos Hakim programmable valve in the treatment of pediatric hydrocephalus.", Childs Nerv Syst, 1997 November-December; 13(11-12):588-93. The ventricular cather and flow-valve are inserted through a scalp incision. The major complications from these and other prior art shunts include infection, obstruction, disconnection, under draining, and over draining, all of which can lead to serious injury and even death. The symptoms of shunt failure and malfunction are nonspecific and include fever, nausea, vomiting, irritability and malaise. A patient presenting to a medical facility with such symptoms warrants a thorough radiological, laboratory, and occasionally a surgical evaluation. As known to those of skill in the art, insertion of CSF shunts requires a highly skilled surgeon or radiologist working under CT X-Ray guidance, but once inserted, such shunts are frequently prone to failure. More recent shunts that attempt to overcome some disadvantages of older shunts include the use of telemetry, as discussed in Miyake H. et al., "A new ventriculpertoneal shunt with a telemetric intracranial pressure sensor: clinical experience in 94 patients with hydrocephalus", Neurosurgery, 1997 May; 40(5): 931-5 and Munshi H., "Intraventricular pressure dynamics in patients with ventriculopleural shunts: a telemetric study", Pedatr Neursurg, 1998 February; 28(2): 67-9 Despite the fact that Miyake and Munshi teach the use of telemetrics with shunts, the shunts taught therein are still prone to failure due to infection, blockages and other difficulties, such that failures of such shunts can still require complete replacement of the shunt.

Web site: http://www.delphion.com/details?pn=US06585677__

- **Synthetic ligation reassembly in directed evolution**

  Inventor(s): Short; Jay M. (Encinitas, CA)

  Assignee(s): Diversa Corporation (San Diego, CA)

  Patent Number: 6,537,776

  Date filed: June 14, 1999

  Abstract: Harvesting the full richness of biodiversity is instantly recognized by Diversa Corporation as a powerful means to access both novel molecules having direct commercial utility as well as molecular templates that could be retooled to acquire commercial utility. A directed evolution process for rapid and facilitated production from a progenitor polynucleotide template, of a library of mutagenized progeny polynucleotides wherein each of the 20 naturally encoded amino acids is encoded at each original codon position. This method, termed site-saturation mutagenesis, or simply saturation mutagenesis, is preferably based on the use of the degenerate N,N,G/T sequence. Also, a method of non-stochastically producing a library of chimeric nucleic acid molecules having an overall assembly order that is chosen by design. Accordingly, a set of progenitor templates, such as genes (e.g. a family of esterase genes) or genes pathways (e.g. encoding antibiotics) can be shuffled to generate a sizable library of distinct progeny polynucleotide molecules (e.g. 10.sup.100) and correspondingly encoded polypeptides. Screening of these polynucleotide libraries enables the identification of a desirable molecular species that has a desirable property, such as a specific enzymatic activity serviceable for a commercial application, or a novel **antibiotic.** Also, a method of retooling genes and gene pathways by the introduction of regulatory sequences, such as promoters, that are operable in an intended host, thus conferring operability to a novel gene pathway when it is introduced into an intended

host. For example a novel man-made gene pathway, generated based on microbially-derived progenitor templates, that is operable in a plant cell.

Excerpt(s): This invention relates to the field of protein engineering. Specifically, this invention relates to a directed evolution method for preparing a polynucleotide encoding a polypeptide. More specifically, this invention relates to a method of using mutagenesis to generate a novel polynucleotide encoding a novel polypeptide, which novel polypeptide is itself an improved biological molecule &/or contributes to the generation of another improved biological molecule. More specifically still, this invention relates to a method of performing both non-stochastic polynucleotide chimerization and non-stochastic site-directed point mutagenesis. Thus, in one aspect, this invention relates to a method of generating a progeny set of chimeric polynucleotide(s) by means that are synthetic and non-stochastic, and where the design of the progeny polynucleotide(s) is derived by analysis of a parental set of polynucleotides &/or of the polypeptides correspondingly encoded by the parental polynucleotides. In another aspect this invention relates to a method of performing site-directed mutagenesis using means that are exhaustive, systematic, and non-stochastic. Furthermore this invention relates to a step of selecting from among a generated set of progeny molecules a subset comprised of particularly desirable species, including by a process termed end-selection, which subset may then be screened further. This invention also relates to the step of screening a set of polynucleotides for the production of a polypeptide &/or of another expressed biological molecule having a useful property.

Web site: http://www.delphion.com/details?pn=US06537776__

- **Transgenic microbial polyhydroxyalkanoate producers**

  Inventor(s): Huisman; Gjalt W. (San Carlos, CA), Peoples; Oliver P. (Arlington, MA), Skraly; Frank A. (Boston, MA)

  Assignee(s): Metabolix, Inc. (Cambridge, MA)

  Patent Number: 6,593,116

  Date filed: August 17, 1999

  Abstract: Transgenic microbial strains are provided which contain the genes required for PHA formation integrated on the chromosome. The strains are advantageous in PHA production processes, because (1) no plasmids need to be maintained, generally obviating the required use of **antibiotics** or other stabilizing pressures, and (2) no plasmid loss occurs, thereby stabilizing the number of gene copies per cell throughout the fermentation process, resulting in homogeneous PHA product formation throughout the production process. Genes are integrated using standard techniques, preferably transposon mutagenesis. In a preferred embodiment wherein mutiple genes are incorporated, these are incorporated as an operon. Sequences are used to stabilize mRNA, to induce expression as a function of culture conditions (such as phosphate concentration), temperature, and stress, and to aid in selection, through the incorporation of selection markers such as markers conferring **antibiotic** resistance.

  Excerpt(s): The present invention is generally in the field of biosynthesis of poly(3-hydroxyalkanoates), and more particularly to improved microbial strains useful in commercial production of polyhydroxyalkanoates. Poly(3-hydroxyalkanoates) (PHAS) are biological polyesters synthesized by a broad range of bacteria. These polymers are biodegradable and biocompatible thermoplastic materials, produced from renewable

resources, with a broad range of industrial and biomedical applications (Williams & Peoples, CHEMTECH 26:38-44 (1996)). PHA biopolymers have emerged from what was originally considered to be a single homopolymer, poly-3-hydroxybutyrate (PHB) into a broad class of polyesters with different monomer compositions and a wide range of physical properties. About 100 different monomers have been incorporated into the PHA polymers (Steinbuchel & Valentin, FEMS Microbiol. Lett. 128:219-28 (1995)). It has been useful to divide the PHAs into two groups according to the length of their side chains and their biosynthetic pathways. Those with short side chains, such as PHB, a homopolymer of R-3-hydroxybutyric acid units, are crystalline thermoplastics, whereas PHAs with long side chains are more elastomeric. The former have been known for about seventy years (Lemoigne & Roukhelman, 1925), whereas the latter materials were discovered relatively recently (deSmet et al., J. Bacteriol. 154:870-78 (1983)). Before this designation, however, PHAs of microbial origin containing both (R)-3-hydroxybutyric acid units and longer side chain (R)-3-hydroxyacid units from C.sub.5 to C.sub.16 had been identified (Wallen & Rohweder, Environ. Sci. Technol. 8:576-79 (1974)). A number of bacteria which produce copolymers of(R)-3-hydroxybutyric acid and one or more long side chain hydroxyacid units containing from five to sixteen carbon atoms have been identified (Steinbuchel & Wiese, Appl. Microbiol. Biotechnol. 37:691-97 (1992); Valentin et al., Appl. Microbiol. Biotechnol. 3:507-14 (1992); Valentin et al., Appl. Microbiol. Biotechnol. 40:710-16 (1994); Abe et al., Int. J. Biol. Macromol. 16:115-19 (1994); Lee et al., Appl. Microbiol. Biotechnol. 42:901-09 (1995); Kato et al., Appl. Microbiol. Biotechnol. 45:363-70 (1996); Valentin et al., Appl. Microbiol. Biotechnol. 46:261-67 (1996); U.S. Pat. No. 4,876,331 to Doi). A combination of the two biosynthetic pathways outlined described above provide the hydroxyacid monomers. These copolymers can be referred to as PHB-co-HX (where X is a 3-hydroxyalkanoate or alkanoate or alkenoate of 6 or more carbons). A useful example of specific two-component copolymers is PHB-co-3-hydroxyhexanoate (PHB-co-3HH) (Brandl et al., Int. J. Biol. Macromol. 11:49-55 (1989); Amos & McInerey, Arch. Microbiol. 155:103-06 (1991); U.S. Pat. No. 5,292,860 to Shiotani et al.).

Web site: http://www.delphion.com/details?pn=US06593116__

- **Treating degenerative disc disease through the transplantation of dehydrated tissue**

  Inventor(s): Ferree; Bret A. (1238 Cliff Laine Dr., Cincinnati, OH 45208)

  Assignee(s): none reported

  Patent Number: 6,648,918

  Date filed: May 10, 2002

  Abstract: A method of treating a diseased or traumatized intervertebral disc is based upon the transplantation of one or more dehydrated biologic tissues into the disc space. In the preferred embodiment, dehydrated nucleus pulposis tissue is used, which may be combined with live nucleus cells. The dehydration allows the insertion of the transplanted cells and/or tissue through a smaller annular hole. Dehydration also decreases the volume of the material transferred, thus allowing the surgeon to insert more into the disc space. Once in the body, the materials hydrate by imbibing fluid from the surrounding area. In the case of nucleus pulposis tissue, the subsequent hydration helps to restore disc height and help prevent extrusion of disc material through the hole in the annulus. One or more therapeutic substances may be added, including culture media, growth factors, differentiation factors, hydrogels, polymers, **antibiotics,** anti-inflammatory medications, or immunosuppressive medications. These additional

substances may or may not be dehydrated as well, depending upon efficacy, initial versus final volume, and so forth.

Excerpt(s): This invention relates generally to the treatment of diseased or traumatized intervertebral discs, and more particularly, to transplantation of transplantation of dehydrated tissue including nucleus pulposis in conjunction with such treatment. Intervertebral discs provide mobility and a cushion between the vertebrae. At the center of each disc is the nucleus pulposus which, in the adult human, is composed of cells and an insoluble extracellular matrix which is produced by the nucleus itself. The extracellular matrix is composed of collagen, proteoglycans, water, and noncollagenous proteins. The nucleus pulposus is surrounded by the annulus fibrosis, which is composed of cells (fibrocyte-like and chondrocyte-like), collagen fibers, and non-fibrillar extracellular matrix. The components of the annulus are arranged in 15-25 lamellae around the nucleus pulposus. The cells of the nucleus pulposus have chondrocyte-like features. In an adult human, the cells of the nucleus pulposis obtain nutrients and eliminate waste by diffusion through blood vessels in the endplates of the vertebrae adjacent to the disc. Blood vessels do not course into the nucleus pulposis. The relative vascular isolation of the nucleus pulposis imparts isolation of nucleus pulposis cells from the body's immune system.

Web site: http://www.delphion.com/details?pn=US06648918__

- **Treatment of behavioral disorders with.beta.-lactam compounds**

  Inventor(s): Koppel; Gary A. (Indianapolis, IN)

  Assignee(s): Revaax Pharmaceuticals, LLC (Indianapolis, IN)

  Patent Number: 6,627,625

  Date filed: August 16, 2000

  Abstract: Administration of.beta.-lactam compounds including.beta.-lactam **antibiotics** and.beta.-lactamase inhibitors provides significant neurotropic effects in warm-blooded vertebrates evidenced inter alia by anxiolytic and anti-aggressive behavior modification and enhanced cognition. Therapeutic methods for using such compounds and their pharmaceutical formulations are described.

  Excerpt(s): This invention relates to a novel mechanism of neuropsychiatric intervention. More particularly, this invention is directed to pharmaceutical formulations and methods for treatment of a variety of neurological disease states, including cognitive and behavioral disorders. The pharmaceutical industry has directed extensive research and development efforts toward discovery and commercialization of drugs for treatment of neurological disorders. Such disorders typically derive from chemical imbalances in the brain. Overproduction or underproduction of pertinent neurochemical species and/or receptor dysfunction has been identified with many disease states recognized by neurologists, psychiatrists, psychologists and other medical practitioners skilled in the diagnosis and treatment of mental disease. Most of the discovery effort for new neurologically active drugs has been based on the study of agonist/antagonist drug interaction with one or more of the numerous receptors in the brain and/or their respective receptor ligands. The present invention provides a novel approach to drug intervention in the treatment of a wide variety of neurologic disease states and other disease states or clinical conditions of related etiology. It is based in part on the discovery that.beta.-lactam containing compounds known for their activity as inhibitors of bacterial peptidases or proteases, particularly transpeptidases and/or

carboxypeptidases, are also potent inhibitors of certain mammalian neuro-peptidases, including N-acetylated-.alpha.-linked acidic peptidases (NAALADases), several of which have been identified/characterized in the literature [Pangalos et al., J. Biol. Chem., 1999, 274, No. 13, 8470-8783]. The present invention is also based in part on the discovery that neurogenic NAALADases can be targeted with NAALADase inhibitors to effect significant behavioral modification and enhanced cognitive performance. Preliminary studies have confirmed that one or more neurogenic proteases, now believed to be NAALADases and related peptidases and transferases, capable of recognizing and transforming certain neuropeptides (e.g., N-acetyl-L-aspartyl-L-glutamate) play a significant if not dominant role at the neurochemical level of brain function and concomitantly have a substantial impact on patient behavior and cognitive performance. It has been previously reported that certain glutamate analogs acting as NAALADase inhibitors can be used to treat prostate disease and glutamate abnormalities associated with certain nervous tissue insult. It has now been determined that NAALADase inhibitors, including particularly certain.beta.-lactam-containing bacterial peptidase and.beta.-lactamase inhibitors capable of blood-brain barrier transport, can function in the brain at very low concentrations as potent neuroactive drug substances to reduce the symptoms of a wide variety of neurological disorders characterized by behavioral aberration or sensory/cognitive dysfunction. Significantly, such bacterial enzyme inhibitors are believed to be effective inhibitors of NAALADase and related neurogenic peptidases, at concentrations below those concentrations known to be required for clinically effective bacterial enzyme inhibition. Thus it is expected that such compounds can also be used effectively for treating prostate disease and the disease states associated with nervous tissue insult previously described as responsive to treatment with other NAALADase inhibitors.

Web site: http://www.delphion.com/details?pn=US06627625__

- **Use of sustained release antibiotic compositions in ophthalmic surgical procedures**

  Inventor(s): Cagle; Gerald D. (Fort Worth, TX), Ke; Tai-Lee (Grand Prairie, TX), Lorenzetti; Ole J. (Fort Worth, TX), Schlech; Barry A. (Fort Worth, TX)

  Assignee(s): Alcon Laboratories, Inc. (Fort Worth, TX)

  Patent Number: 6,630,135

  Date filed: November 12, 1999

  Abstract: An improved method of sterilizing the field of surgery prior to an ophthalmic surgical procedure is described. The invention eliminates the need for painful and potentially traumatic injections of **antibiotics** by utilizing sustained release compositions which allow the **antibiotics** contained therein to penetrate deeply into the eye, thereby ensuring a sterile field of surgery during intraocular surgical procedures. The compositions may also be utilized to prevent post-surgical infections.

  Excerpt(s): The present invention relates to sustained release pharmaceutical compositions containing one or more **antibiotics.** The invention is also directed to the use of such compositions to sterilize the tissues in the area of surgery (i.e., the "surgical field" or "field of surgery") prior to a surgical procedure and to prevent post-surgical infections. Ophthalmic surgical procedures currently involve the topical application of betadine solution to the eyelid and other tissues adjacent to the eye prior to surgery. The preoperative procedures may also include topical instillation of argyrol to facilitate removal of mucus and other debris present on the cornea and conjunctiva. However, the foregoing procedures do not result in sterilization of the ophthalmic tissues which form

the site of the surgery (e.g., the cornea, sclera or various other ophthalmic tissues). Antimicrobial agents such as the aminoglycosides, penicillins and cephalosporins, being relatively insoluble in lipids, penetrate the eye poorly after systemic administration. Therefore, the surgical field is currently sterilized by subconjunctival injection of any one of various **antibiotics.** The most commonly used drug in subconjunctival injection is gentamicin (about 30 mg per injection). This method involves the insertion of a 20 gauge needle into the subconjunctival space, taking care not to pierce the conjunctiva; 0.1 ml to 1.0 ml of **antibiotic** is injected. This technique permits significant **antibiotic** to enter the corneoscleral limbus near the subconjunctival injection site. However, such injections present a significant risk of injury to ophthalmic tissues if performed improperly. Even when proper procedures are followed, such injections are painful and inherently involve at least some undesirable trauma due to the passing of the hypodermic needle through very delicate ophthalmic tissues. In addition, subconjunctival injections of **antibiotics** can result in nonuniform concentrations of the **antibiotics** in the cornea, and the concentrations attained may be inadequate. For example, the maximum gentamicin concentration attained in the aqueous humor of rabbits from subconjunctival injection is 8.8 ug/g. Although a concentration of 8.8 ug/g would be effective against some bacteria, a significantly higher concentration is required for more resistant strains. Still another problem is the fairly recent development of bacterial resistance to aminoglycoside **antibiotics.**

Web site: http://www.delphion.com/details?pn=US06630135__

- **Water-soluble compositions of bioactive lipophilic compounds**

  Inventor(s): Borowy-Borowski; Henryk (Ottawa, CA), Sikorska-Walker; Marianna (Navan, CA), Walker; P. Roy (Navan, CA)

  Assignee(s): National Research Council of Canada (Ottawa, CA)

  Patent Number: 6,632,443

  Date filed: February 2, 2001

  Abstract: Water-soluble compositions comprising a lipophilic compound and a solubilizing agent of the general formula:{X--OOC--[(CH.sub.2).sub.n --COO].sub.m }.sub.p --Y (I)wherein:X is a residue of a hydrophobic moiety,Y is a residue of a hydrophilic moiety,p is 1 or 2,m is 0 or 1, andn is an integer greater than or equal to 0are disclosed. The lipophilic compound is preferably selected from the group consisting of water-insoluble ubiquinones, ubiquinols, vitamins, provitamins, polyene macrolide **antibiotics,** and mixtures thereof. The hydrophobic moiety is preferably a sterol or a tocopherol and the hydrophilic moiety is preferably a polyalkylene glycol. In some embodiments, the sterol is cholesterol or sitosterol, the tocopherol is.alpha.-(+)-tocopherol, the polyalkylene glycol is a polyethylene glycol or its methyl monoether having an average molecular weight between 400 and 1000, p is equal to 1 or 2, m is equal to 0 or 1 and n is an integer between 2 and 18.

  Excerpt(s): The present invention relates to water-soluble compositions of bioactive lipophilic compounds, to compounds useful for the preparation of such compositions, to methods of preparing such compounds and compositions, and to the use of such compositions as therapeutics and cosmetics. Many bioactive compounds are highly lipophilic (hydrophobic), meaning that they are soluble in lipids (oils) and some organic solvents, while being substantially insoluble or only sparsely soluble in water. The lack of solubility of a bioactive compound in aqueous media is an important factor limiting its therapeutic applications, making difficult an efficient administration of the

compound to a patient. When administered in the form of an oil solution or some kind of water and/or oil suspension or emulsion, lipophilic compounds usually show a poor bioavailability, meaning a low concentration and a long build-up time of the compound in the systemic circulation. This lack of bioavailability is usually independent of the administration route (topical, oral, or parenteral). Various approaches to overcoming this limitation are known in the prior art. One known approach consists of dissolving a lipophilic compound in a water-miscible organic solvent, such as ethanol or propylene glycol. When such a solution is admixed with blood or gastrointestinal fluids, however, the lipophilic compound usually precipitates as a solid or liquid emulsion, with a resulting low bioavailability. Furthermore, for many lipophilic compounds no organic, water-miscible solvents exist. Another approach consists of incorporating lipophilic compounds into various compositions, frequently inhomogeneous, multiphase emulsions, containing oils and solvents in combination with surfactants. These compositions may improve the bioavailability of the compound without significantly increasing its solubility in aqueous media, but are normally suitable only for a particular administration form, usually for topical applications. Such compositions, which may also induce a protective immune response in mammals, are of little value for therapeutic uses where administration of the compound by ingestion or injection is necessary and where an aqueous solution or a water-soluble solid composition is frequently the only acceptable administration form.

Web site: http://www.delphion.com/details?pn=US06632443__

## Patent Applications on Antibiotics

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 antibiotics:

- **Antibiotic pharmaceutical composition with lysergol as bio-enhancer and method of treatment**

  Inventor(s): Arya, Jai Shankar; (Lucknow, IN), Darokar, Mahendra Pandurang; (Lucknow, IN), Kumar, Sushil; (Lucknow, IN), Santha Kumar, Tiruppadiripuliyur Ranganathan; (Lucknow, IN), Shasany, Ajit Kumar; (Lucknow, IN), Singh Khanuja, Suman Preet; (Lucknow, IN), Srivastava, Santosh Kumar; (Lucknow, IN)

  Correspondence: Norman H. Stepno, Esquire; BURNS, DOANE, SWECKER & MATHIS, L.L.P.; P.O. Box 1404; Alexandria; VA; 22313-1404; US

  Patent Application Number: 20030181425

  Date filed: March 25, 2002

  Abstract: The present invention relates to pharmaceutical composition with lysergol as bioactive enhancer and bioavailability facilitator for broad-spectrum **antibiotics.** The present invention has direct implication in reducing the dosage of **antibiotics** while increasing the efficiency of absorption of nutritional elements.

  Excerpt(s): The invention relates to a synergistic **antibiotic** pharmaceutical composition with lysergol as bioactive enhancer and bioavailability facilitator for broad-spectrum

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

**antibiotics.** The present invention has direct implication in reducing the dosage of **antibiotics** while increasing the efficiency of absorption of nutritional elements. The present invention also provides a method of treatment for bacterial infections. The consumption of **antibiotics** and drugs by man is increasing at an alarming rate. Out of the total drugs and chemicals, 20%-50% of that use is unnecessary depending on the class of **antibiotic.** In addition, indiscriminate use of **antibiotics** promotes **antibiotic** resistance leading to multiple drug resistance and makes it difficult to control the diseases. Really speaking, the infected individuals consume much more amount of **antibiotics** in the given dosage that is actually required to control a given population of parasite in the body. This may be due to (i) reduced absorption in the gut membrane when taken orally (ii) restrictive uptake by the target microbe or (iii) operation of efflux pump leading to indiscriminate extrusion of the **antibiotics** or therapeutic molecules. So the major amount of the drugs we apply are wasted and only a minor percentage is being targeted to the infective microbes. In addition, the unutilized drug/antibiotic amount remains as a load in the body and environment acting as a selection pressure facilitating emergence of drug resistance in parasites and their predominance, ultimately leading to failure of **antibiotics** against resistant infections. This also is responsible for side effects, illness and reduction in life expectancy. One of the ways, which has been feasible to reduce drug dosage, has been synergism between two therapeutic agents. However, if both have the **antibiotic** property, still the problem of continued selection pressure on microbes is likely to continue. So, we thought of searching only those molecules, which by them are not microbicidal but when present with a drug or active molecule, enhance its activity and availability (bioenhancers). This way these molecules by their presence will not exert any selection pressure for mutants to emerge resistant against them and on the other hand could reduce the dosage of **antibiotics** or drugs so that their ill effects are minimized and the resistance development process will be substantially delayed ultimately leading to enhanced life-span of the novel and existing **antibiotics.** Such drug/molecule facilitators should have novel properties like non-toxic to human, animal or plants, should be effective at a very low concentration in a combination, should be easy to formulate and most importantly enhance uptake/absorption and activity of the drug molecules. This can lead in developing judicious and strategic concentrations of **antibiotics** with specific bioenhancers to improve availability of the drug right up to the target for effectively controlling the infectious organisms. The present invention was the result of planned experiments to provide a plant compound `Lysergol` with novel properties for improving activity and bioavailability of **antibiotics,** drugs and other molecules in different formulations. The bioavailability enhancement of **antibiotic** effect is relevant to human, plant as well as animal health and thus the compositions and methods of the invention are also intended to be used in agriculture and veterinary practice.

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

- **Antibiotics for treating biohazardous bacterial agents**

  Inventor(s): Cassell, Gail Houston; (Carmel, IN), Nicas, Thalia Ioanna; (Indianapolis, IN)

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  Patent Application Number: 20030176327

  Date filed: October 18, 2002

Abstract: The present invention is directed to methods for the control of strains of bio-hazardous bacterial agents. These agents include: Bacillus anthracis, Yersinia Pestis, Francisella tularensis, Clostridium botulinin, Clostridium Perfringens, Brucella abortis, B milletensis, B suis and Burkholderia mallei. These methods employ treating an infected warm-blooded animal with an **antibiotics** selected from: Cephalothin, Cefazolin, Cephalexin monohydrate, Cephalexin HCl, Cefaclor, Loracarbef, Erythromycin estolate, Dirithromycin, Cinoxacin, Vancomycin HCl, Tobramycin, Cefamandole, Cefuroxime, Daptomycin, and Oritavancin.

Excerpt(s): Of the numerous bio-hazardous bacterial agents that may be used as weapons, there are a limited number of organisms that could cause disease and deaths in sufficient numbers to cripple a city or region. These organisms include: Bacillus anthracis, Yersinia Pestis, Francisella tularensis, Clostridium botulinin, Clostridium, Perfringens, Brucella abortis, B milletensis, B suis and Burkholderia mallei. Anthrax, attributable to infection with Bacillus anthracis, is among the most serious diseases that can be contracted from a bio-hazardous agent. Biological agents have seldom been dispersed in aerosol form, the exposure mode most likely to inflict widespread disease. Therefore, historical experience provides little information about the potential impact of a biological attack or the possible efficacy of postattack measures such as vaccination, **antibiotic** therapy, or quarantine. For centuries, anthrax has caused disease in animals and, uncommonly, serious illness in humans throughout the world. (see D. Lew , Bacillus anthracis (anthrax); in G. L. Mandell, J. E. Bennett, R. Dolin, eds.; Principles and Practices of Infectious Disease, New York, N.Y.; Churchill Livingstone Inc; 1885-1889 (1989)). Research on anthrax as a biological weapon began more than 80 years ago. (see G. W. Christopher, T. J. Cieslak, J. A. Pavlin, and E. M. Eitzen, "Biological warfare: a historical perspective," JAMA 278, 412-417 (1997)). Today, at least 17 nations are believed to have offensive biological weapons programs (see L. A. Cole, "The specter of biological weapons," Sci.Am., 60-65 (December 1996)); it is uncertain how many are working with anthrax. Iraq has acknowledged producing and weaponizing anthrax. (see R. A. Zalinskas, "Iraq's biological weapons: the past as future?," JAMA 278, 418-424 (1997)).

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

- **Antibiotics, tripropeptins and process for producing the same**

Inventor(s): Hamada, Masa; (Tokyo, JP), Hashizume, Hideki; (Tokyo, JP), Igarashi, Masayuki; (Kanagawa, JP), Naganawa, Hiroshi; (Tokyo, JP), Takeuchi, Tomio; (Tokyo, JP)

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Patent Application Number: 20030162697

Date filed: November 7, 2002

Abstract: By culturing Lysobacter sp. BMK333-48F3 (deposit number of FERM BP-7477), an **antibiotic,** tripropeptin Z, tripropeptin A, tripropeptin B, tripropeptin C or tripropeptin D represented by the general formula (I): 1wherein R is 7-methyl-octyl group, 8-methyl-nonyl group, 9-methyl-dodecyl group, 10-methyl-undecyl group or 11-methyl-dodecyl group, is obtained as **antibiotics** having excellent antibacterial activities against bacteria and having a novel molecular structure. These tripropeptins each have an excellent antibacterial activity against various bacteria and drug-resistant strains thereof, such as methicillin-resistant strains and vancomycin-resistant strains.

Excerpt(s): This invention relates to new **antibiotics,** namely tripropeptins Z, A, B, C and D or pharmaceutically acceptable salts thereof, which each have excellent antibacterial activities. This invention also relates to a process for producing a tripropeptin. Further, this invention relates to a pharmaceutical composition, particularly an antibacterial composition, comprising a tripropeptin or a pharmaceutically acceptable salt thereof as an active ingredient. Still further, this invention relates to Lysobacter sp. BMK333-48F3, as a new microorganism, having a characteristic nature that it is capable of producing a tripropeptin. As **antibiotics** were commonly used, multi-drug-resistant bacteria, particularly methicillin-resistant bacteria have widely occurred and these resistant bacteria have brought about a clinical problem. The methicillin-resistant bacteria can exhibit a resistance not only against methicillin but also against many **antibiotics** such as **antibiotics** of aminoglycosides, tetracyclines,.beta.-lactams and macrolides. In recent years, drug-resistant bacteria have appeared even against vancomycin which is an **antibiotic** known as a last remaining card for the therapy of infections of the methicillin-resistant bacteria. Thus, there is now a keen request for finding and providing a novel compound which can exhibit excellent antibacterial activities against the drug-resistant bacteria, particularly the methicillin-resistant bacteria and vancomycin-resistant bacteria.

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

- **Apparatus and method for surface culture of microorganisms from bulk fluids**

  Inventor(s): Hyman, Jones M.; (Durham, NC), Jeffrey, Scott R.; (Raleigh, NC), Maresch, Martin J.; (Willmar, MN), Matsumura, Paul M.; (Cary, NC), Thorpe, Thurman C.; (Durham, NC)

  Correspondence: Samir R. Patel, Esq.; bioMerieux, Inc.; Patent Department; 100 Rodolphe Street; Durham; NC; 27712; US

  Patent Application Number: 20030203477

  Date filed: May 2, 2003

  Abstract: A device and method are provided for isolating and culturing microorganisms from a bulk fluid sample. The device comprises a container having therein a polymeric immobilization layer having interstitial spaces between polymer chains such as a gel matrix. The interstitial spaces are of an average size less than an average size of microorganisms to be separated from the sample and cultured. A bulk fluid sample is applied to the immobilization layer where fluid is absorbed by the layer and microorganisms remain on the surface of the layer. After culturing, microorganism colonies are readily accessible on the surface of the layer for harvest and testing. The immobilization layer may contain one or more of nutrients for microorganisms growth, lytic agents, lytic enzymes, **antibiotics, antibiotic** neutralizers, indicators, detergents and selective agents. An adjacent support layer may be above and/or below the immobilization layer. The immobilization layer may be in combination with a sensor layer that changes color in areas corresponding to portions of the layer having microorganisms thereon. A membrane may be embedded in the immobilization layer for enhancing microorganism visibility and facilitating microorganism harvest.

  Excerpt(s): This application is related to U.S. patent application Ser. No. 08/989,560 to Jeffrey et al. filed Dec. 12, 1997, and U.S. patent application Ser. No. 09/113,929 to Maresch et al. (now U.S. Pat. No. 5,912,115), the subject matter of each being incorporated herein by reference. The presence of microbial contamination in clinical specimens is conventionally determined by culturing the specimens in the presence of

nutrients and detecting microbial activity through changes in the specimen or in the atmosphere over the specimen after a period of time. For example, in the U.S. Pat. No. 4,182,656 to Ahnell et al., the sample is placed in a container with a culture medium comprising a carbon 13 labeled fermentable substrate. After sealing the container and subjecting the specimen to conditions conducive to biological activity, the ratio of carbon 13 to carbon 12 in the gaseous atmosphere over the specimen is determined and compared with the initial ratio. In U.S. Pat. No. 4,152,213, a method is claimed by which the presence of oxygen consuming bacteria in a specimen is determined in a sealed container by detecting a reduction in the amount of oxygen in the atmosphere over the specimen through monitoring the pressure of gas in the container. U.S. Pat. No. 4,073,691 provides a method for determining the presence of biologically active agents, including bacteria, in a sealed container containing a culture medium by measuring changes in the character of the gaseous atmosphere over the specimen after a period of time. A method for non-invasive detection is taught by Calandra et al., U.S. Pat. No. 5,094,955, where a device is disclosed for detecting the presence of microorganisms in clinical specimens, such as blood or other body fluids, and in non-clinical specimens, by culturing the specimens with a sterile liquid growth medium in a transparent sealed container. The presence of microorganisms is determined by detecting or measuring changes in the pH of the specimen or the production of carbon dioxide within the specimen using a sensor affixed to the interior surface of the container or to the sealing means used to seal the container. In Calandra et al., microorganisms can be detected in the presence of interfering material, such as large concentrations of red blood cells, through non-radiometric and non-invasive means.

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

- **Bifunctional antibiotics**

  Inventor(s): Sucheck, Steven; (San Diego, CA), Wong, Chi- Huey; (Rancho Santa Fe, CA)

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  Patent Application Number: 20030181399

  Date filed: March 28, 2003

  Abstract: Bifunctional **antibiotics** that target both bacterial RNA and resistance-causing enzymes are disclosed. The A-site of bacterial 16S rRNA serves as the target site for most aminoglycoside **antibiotics.** Resistance to this class of **antibiotics** is frequently developed by microbial enzymatic acetylation, phosphorylation or ribosylation of aminoglycosides, modifications that weaken their interactions with the target RNA. Using surface plasmon resonance (SPR), the binding affinity and stoichiometry of various amino-glycosides have been investigated and it was found that neamine, the key pharmacophore of the deoxystreptamine class of amino-glycosides, binds to the A-site in a two to one stoichiometry with a K.sub.d of 10.mu.M for each binding site. A library of neamine dimers was prepared and their affinities to 16S rRNA A-site were determined by SPR, with K.sub.d=40 nM for the best dimer (an.about.10.sup.3-fold increase in affinity). **Antibiotic** activities of the dimers were determined for several bacterial strains by the Kirby-Bauer method. The most active dimer, based on **antibiotic** activity, also showed the highest inhibition of in vitro translation (IC.sub.50=0.055.mu.M). The latter assay was developed in order to correlate the relationship between SPR-based affinity and translation inhibition. By these combined methods, transport limitations for the semisynthetic aminoglycosides as well as non-

ribosomally based **antibiotic** activity could be determined. Further analysis of these dimers as substrates for aminoglycoside modifying-enzymes identified a neamine dimer that was a potent inhibitor (K.sub.is=0.1.mu.M) of the APH(2") activity of the bifunctional enzyme AAC(6")-APH(2"), the primary enzyme responsible for high level gentamicin C resistance in several bacterial strains.

Excerpt(s): The invention relates to bifunctional **antibiotics.** More particularly, the invention related to bifunctional **antibiotics** that target bacterial rRNA and inhibit resistance-causing enzymes. Deoxystreptamine-based aminoglycosides are a clinically important class of **antibiotics** that are effective against a broad range of microorganisms (Edson, R. S.; Terrel, C. L. Mayo Clin. Proc. 1991, 66, 1158). It is believed that aminoglycosides exert their therapeutic effect by interfering with translational fidelity during protein synthesis via interaction with the A-site rRNA on the 16S domain of the ribosome (Moazed, D.; Noller, H. F. Nature 1987, 327, 389; Purohit, P.; Stern, S. Nature 1994, 370, 659; Formy, D.; et al. Science 1996, 274, 1367). Unfortunately, the high toxicity and rapid emergence of high level aminoglycoside resistance have severely limited the usefulness of this class of **antibiotics.** Numerous aminoglycoside resistance mechanisms have been identified, and enzymatic acetylation, phosphorylation and ribosylation are the primary causes of high level resistance in most clinical isolates (Wright, G. D.; et al. Adv. Exp. Med. Biol. 1998, 456, 27; Kondo, S.; Hotta, K. J. Infect. Chemother. 1999, 5, 1; Mingeot-Leclerco, M.-P.; et al. Antimicrob. Agents Chemother. 1999, 43, 727). Of the modifying enzymes, the acetyl- and phosphotransferases (AAC and APH) have been extensively studied with respect to their specificity (Wright, G. D.; et al. Adv. Exp. Med. Biol. 1998, 456, 27; Kondo, S.; Hotta, K. J. Infect. Chemother. 1999, 5, 1; Mingeot-Leclerco, M.-P.; et al. Antimicrob. Agents Chemother. 1999, 43, 727; Daigle, D. M.; et al. Chem. Biol. 1999, 6, 99; Azucena, E.; et al. J. Am. Chem. Soc. 1997, 119, 2317; Patterson, J.-E.; Zervos, M. J. Rev. Infect. Dis. 1990, 12, 644). What was needed was a method to tackle the problem of **antibiotic** resistance. What was needed was bifunctional aminoglycosides that can resist or inhibit aminoglycoside-modifying enzymes while simultaneously targeting ribosomal RNA.

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

- **Bifunctional glycopeptide antibiotics and combinatorial libararies thereof**

  Inventor(s): Chen, Zhong; (Princeton, NJ), Kahne, Daniel; (Princeton, NJ), Sun, Binyuan; (Princeton, NJ)

  Correspondence: WOODCOCK WASHBURN LLP; ONE LIBERTY PLACE, 46TH FLOOR; 1650 MARKET STREET; PHILADELPHIA; PA; 19103; US

  Patent Application Number: 20030158093

  Date filed: August 19, 2002

  Abstract: The present invention relates to a the design of a large class of **antibiotics** comprised of aglycones of vancomycin or derivatives of an aglycone of vancomycin attached to the anomeric site of moenomycin or a moenomycin derivative.

  Excerpt(s): This application claims benefit of provisional application serial No. 60/313,271, filed Aug. 17, 2001, the disclosure of which is hereby incorporated by reference in its entirety. The present inventions relate to the design of a large class of new **antibiotics** comprised of an aglycone of vancomycin or a derivative of the aglycone of vancomycin attached to the anomeric carbon of moenomycin or a moenomycin derivative. The emergence of resistance to vancomycin in enterococcal strains has

aroused considerable concern. See e.g., Walsh, C. T., Nature 2000, 406 775. Efforts to overcome resistance have led to the development of a new class of vancomycin derivatives containing hydrophobic substituents on the vancosamine sugar. Nagaraj an, R., J. Antibiot. 1993, 46, 118. These glycolipid derivatives are more active than vancomycin against both sensitive and resistant enterococcal strains. It is possible that these glycolipid derivatives of vancomycin are bifunctional molecules, consisting of two biologically active components that interact with different cellular targets. See Ge, M. et al., Science, 1999, 284, 507; Kerns, R. et al., J. Am. Chem. Soc., 2000, 122, 12608. The aglycone binds to the D-Ala-D-Ala dipeptide terminus of peptidoglycan precursors and the substituted disaccharide interacts with proteins involved in the transglycosylation step of peptidoglycan synthesis. This is one possible mechanism for how the compounds overcome resistance. Other mechanisms have been proposed and tested. See e.g., Williams, D. H. et al., Angew. Chem. Int. Ed., 1999, 38, 1172; Rao, J. et al., Science, 1998, 280, 708; Sundram, U. N. et al., J. Am. Chem. Soc., 1996, 118, 13107; Nicolaou, K. C. et al., Angew. Chem. Int. Ed., 2000, 39, 3823.

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

- **BRANCHED CHAIN AMINO ACID-DEPENDENT AMINOTRANSFERASE INHIBITORS AND THEIR USE IN THE TREATMENT OF NEURODEGENERATIVE DISEASES**

  Inventor(s): Hays, Sheryl Jeanne; (Ann Arbor, MI), Hu, Lain-Yen; (Ann Arbor, MI), Lei, Huangshu; (Ann Arbor, MI), Scholten, Jeffrey David; (Ann Arbor, MI), Wustrow, David Juergen; (Ann Arbor, MI)

  Correspondence: WARNER-LAMBERT COMPANY; 2800 PLYMOUTH RD; ANN ARBOR; MI; 48105; US

  Patent Application Number: 20030162779

  Date filed: November 26, 2002

  Abstract: The invention relates to BCAT inhibitors and the use thereof for treating or preventing neuronal loss associated with stroke, ischemia, CNS trauma, hypoglycemia and surgery, as well as treating neurodegenerative diseases including Alzheimer's disease, amyotrophic lateral sclerosis, Huntington's disease and Down's syndrome, treating or preventing the adverse consequences of the overstimulation of the excitatory amino acids, treating anxiety, psychosis, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine headache, chronic pain, neuropathic pain, Parkinson's disease, diabetic retinopathy, glaucoma, CMV retinitis, urinary incontinence, opioid tolerance or withdrawal, and inducing anesthesia, as well as for enhancing cognition.

  Excerpt(s): This application claims benefit of U.S. Provisional Application No. 60/333,593 filed Nov. 27, 2001. This invention is related to branched chain amino acid-dependent amino transferase (BCAT) inhibitors. The invention is also directed to the use of BCAT inhibitors as neuro-protective agents for treating conditions such as stroke, cerebral ischemia, central nervous system trauma, hypoglycemia, anxiety, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine headaches, chronic pain, neuropathic pain, glaucoma, CMV retinitis, diabetic retinopathy, psychosis, urinary incontinence, opioid tolerance or withdrawal, or neuro-degenerative disorders such as lathyrism, Alzheimer's disease, Parkinsonism, amyotrophic lateral sclerosis (ALS), and Huntington's Disease. Excessive excitation by neurotransmitters can cause the degeneration and death of neurons. It is believed that this degeneration is in part mediated by the excitotoxic actions of the excitatory amino acids (EAA) glutamate and

aspartate at the N-methyl-D-aspartate (NMDA) receptor. This excitotoxic action is considered responsible for the loss of neurons in cerebrovascular disorders such as cerebral ischemia or cerebral infarction resulting from a range of conditions, such as thromboembolic or hemorrhagic stroke, cerebral vasospasms, hypoglycemia, cardiac arrest, status epilepticus, perinatal asphyxia, anoxia such as from drowning, pulmonary surgery and cerebral trauma, as well as lathyrism, Alzheimer's disease, Parkinson's disease, and Huntington's disease.

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

- **Combination therapy for the treatment of bacterial infections**

  Inventor(s): Hafkin, Barry; (Danbury, CT), Needleman, Philip; (Creve Coeur, MO)

  Correspondence: PHARMACIA & UPJOHN; 301 HENRIETTA ST; 0228-32-LAW; KALAMAZOO; MI; 49007; US

  Patent Application Number: 20030191051

  Date filed: January 21, 2003

  Abstract: The present invention provides compositions and methods for treating or preventing bacterial infections. The compositions and methods include the use of **antibiotics** and cyclooxygenase inhibitors.

  Excerpt(s): This application claims the benefit of the following provisional application(s): U.S. Serial No. 60/351,058, filed January 23, 2002, under 35 USC 119(e)(i). Antibiotics were introduced into medical practice nearly 50 years ago. **Antibiotics** have been used to control many life-threatening diseases, to reduce death and illness, and to increase the life expectancy of the population. However, the benefits of **antibiotics** have not been gained without the introduction of some associated problems. Antibiotics are commonly administered to treat bacterial infections by, for example, injection, oral administration, or application to the skin in ointment form. Many **antibiotics** are potent anti-infective agents, but also cause toxic side effects. For example, penicillin is highly allergenic and can cause skin rashes, shock, and other allergic responses. Tetracyclines are capable of causing major changes in the intestinal bacterial population and can result in superinfection by fungi and other microorganisms. Chloramphenicol is known to produce severe blood diseases, which has led to restrictions in its use. Streptomycin can result in ear and kidney damage. Moreover, many **antibiotics** have lost their effectiveness against some bacterial diseases and, as a result, some illnesses that were once easily treatable now pose treatment problems for physicians and their patients.

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

- **Combinatorial polyketide libraries produced using a modular PKS gene cluster as scaffold**

  Inventor(s): Kao, Camilla M.; (Palo Alto, CA), Khosla, Chaitan; (Palo Alto, CA)

  Correspondence: Brenda J. Wallach; Morrison & Foerster LLP; Suite 500; 3811 Valley Centre Drive; San Diego; CA; 92130-2332; US

  Patent Application Number: 20030170725

  Date filed: August 6, 2002

Abstract: Combinatorial libraries of polyketides can be obtained by suitable manipulation of a host modular polyketide synthase gene cluster such as that which encodes the PKS for erythromycin. The combinatorial library is useful as a source of pharmaceutically active compounds. In addition, novel polyketides and **antibiotics** are prepared using this method.

Excerpt(s): This application is a continuation-in-part of U.S. Ser. No. 08/846,247 filed Apr. 30, 1997 which is a continuation-in-part of U.S. Ser. No. 08/486,645 filed Jun. 7, 1995 which is continuation-in-part of U.S. Ser. No. 08/238,811 filed May 6, 1994. Priority is claimed under 35 USC.sctn.120. Priority is also claimed under 35 USC 119(e) with respect to U.S. Provisional application No. 60/076,919 filed Mar. 5, 1998. The disclosures of these applications are incorporated herein by reference. The invention relates to the field of combinatorial libraries, to novel polyketides and **antibiotics** and to methods to prepare them. More particularly, it concerns construction of new polyketides and to libraries of polyketides synthesized by polyketide synthases derived from a naturally occurring PKS, as illustrated by the erythromycin gene cluster. Polyketides represent a large family of diverse compounds ultimately synthesized from 2-carbon units through a series of Claisen-type condensations and subsequent modifications. Members of this group include **antibiotics** such as tetracyclines, anticancer agents such as daunomycin, and immunosuppressants such as FK506 and rapamycin. Polyketides occur in many types of organisms including fungi and mycelial bacteria, in particular, the actinomycetes.

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

- **Composition and method for dermatological treatment**

  Inventor(s): Patel, Pravin M.; (Bloomfield Hills, MI)

  Correspondence: GIFFORD, KRASS, GROH, SPRINKLE; ANDERSON & CITKOWSKI, PC; 280 N OLD WOODARD AVE; SUITE 400; BIRMINGHAM; MI; 48009; US

  Patent Application Number: 20030215493

  Date filed: April 30, 2003

  Abstract: A topical composition for the treatment of acne and other dermatological conditions comprises a liposomal formulation of a retinoid and an **antibiotic** in which the retinoid is disposed in the lipid phase of the formulation, and the **antibiotic** is disposed in the aqueous phase. Lincosamides, such as clindamycin, are one group of **antibiotics** which may be used in the composition. Tretinoin is one preferred retinoid. Also disclosed are methods for making the compositions and methods for using the composition.

  Excerpt(s): This patent application claims priority of U.S. Provisional Patent Application Serial No. 60/377,002 filed Apr. 30, 2002, entitled "Composition and Method for Dermatological Treatment". This invention relates generally to the treatment of skin conditions such as acne. More specifically, the invention relates to dermatological compositions based upon liposomal formulations of retinoids and **antibiotics,** and their use for the treatment of acne. Acne is a dermatological disorder which occurs when inflamed sebaceous glands become blocked with sebum, skin cells and bacteria. Lesions occur in more superficial forms as open or closed comedones, as well as in deeper varieties such as nodules and cysts. Acne tends to appear at the onset of puberty and persists into early adulthood. One reason for the association of acne with puberty is that sebum levels are under hormonal control. While not usually physically disabling, acne

can be particularly disturbing for cosmetic reasons to those affected. In addition, untreated or inappropriately treated acne can result in permanent, disfiguring scarring.

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

- **Compositions and methods for treating inflammatory connective tissue diseases**

  Inventor(s): Moskowitz, Roland W.; (Pepper Pike, OH)

  Correspondence: Barbara E. Arndt, Ph.D.; Jones Day; North Point; 901 Lakeside Avenue; Cleveland; OH; 44114; US

  Patent Application Number: 20030207819

  Date filed: May 2, 2003

  Abstract: The invention provides compositions and methods utilizing 14- and 15-member macrolide **antibiotics** for the treatment of patients with connective tissue diseases. The methods of the invention provide for the administration to a patient of a therapeutically effective amount of a 14-member macrolide **antibiotic,** a 15-member macrolide **antibiotic,** pharmaceutically acceptable derivatives thereof, and combinations thereof for a period of time sufficient to obtain a desired alleviation of one or more symptoms of the connective tissue disease.

  Excerpt(s): This application claims the benefit of U.S. Ser. No. 60/377,281 filed May 2, 2002, which disclosure is incorporated herein by reference. Although the exact etiology of most inflammatory rheumatic and other chronic inflammatory connective tissue diseases is uncertain, it is known that immunoregulatory abnormalities can lead to vascular and cellular injury from the action of leukocytes and the mediators of inflammation that they produce. The accumulation of these cells is mediated by the same mechanisms involved in the normal response to bacterial invasion. Abnormal regulation of cytokine production by leukocytes, manifested by overproduction of inflammatory cytokines and/or decreased production of anti-inflammatory cytokines, can play a key role in the pathogenesis of immune-mediated diseases. For example, rheumatoid arthritis is characterized by increased levels of the inflammatory cytokines IL-1.beta., TNF.alpha., and IL-6, and decreased levels of the anti-inflammatory cytokine, IL-10. Similar cytokine profiles can be found in other inflammatory arthritides. Adhesion molecules (cell surface molecules essential to cell-to-cell interaction during immune activation and cell migration and recruitment) such as ICAM- 1, VCAM- 1, LFA- 1, E-selectin, and the like, are involved to various degrees in the pathogenesis of many rheumatic diseases including rheumatoid arthritis, giant cell arteritis, psoriatic arthritis and others. The release of nitric oxide, superoxide radicals, and other toxic oxygen metabolites (the respiratory burst) by neutrophils, disordered apoptosis (programmed cell death), and production of prostaglandins can also contribute to tissue injury.

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

- **Compositions and methods for treatment of staphylococcal infection while suppressing formation of antibiotic-resistant strains**

  Inventor(s): Archer, Gordon; (Richmond, VA), Climo, Michael; (Richmond, VA), Murphy, Ellen; (Bronx, NY)

  Correspondence: Supervisor, Patent Prosecution Services; PIPER RUDNICK LLP; 1200 Nineteenth Street, N.W.; Washington; DC; 20036-2412; US

  Patent Application Number: 20030199432

  Date filed: April 16, 2003

  Abstract: Co-administration of a lysostaphin or other anti-staphylococcal agent which cleaves cross-links of peptidoglycans of staphylococci cell walls such as lysostaphin and an **antibiotic** effective against staphylococci due to **antibiotic** activity mediated by cell-wall activity is effective against staphylococcal infection, even staphylococci that may be resistant to one or other of lysostaphin or the cell-wall active **antibiotic.** Co-administration simultaneously suppresses the generation of antibiotic-resistant mutant strains. Effective cell-wall active **antibiotics** include.beta.-lactams and glycopeptides.

  Excerpt(s): This invention pertains to a method of treating staphylococcal infection in mammals, including humans. The method involves the simultaneous administration of a lysostaphin or other agent which attacks the glycine-containing peptide cross-links of the cell wall peptidoglycan found in staphylococci and an **antibiotic,** the **antibiotic** properties of which are mediated by its ability to affect the cell wall of the target staphylococci. This combined administration is effective in treating the staphylococcal infection, and at the same time suppresses the formation of strains resistant to lysostaphin or other peptidoglycan active agent. Lysostaphin is a bacteriocin secreted by a staphylococcal strain isolated and originally named Staphylococcus staphylolyticus (now S. simulans). The production oflysostaphin is described in U.S. Pat. 3,278,378. Lysostaphin is an endopeptidase which cleaves the polyglycine cross-links of the peptidoglycan found in the cell walls of staphylococci. U.S. Pat. Nos. 3,398,056 and 3,594,284 describe improvements to culture medium and inoculation techniques for the production of lysostaphin. The gene for lysostaphin from S. simulans has been sequenced and cloned, U.S. Pat. No.4,931,390. Lysostaphin for use as a laboratory reagent has been produced by fermentation of a non-pathogenic recombinant strain of B. sphaericus, from which it is readily purified. The cloning and sequencing of the lysostaphin gene permits the isolation of variant enzymes that have properties similar to or different from those of wild type lysostaphin. One such altered enzyme, bearing a single amino acid change, has been characterized and shown to have potent anti-staphylococcal activity both in vitro and in an animal infection model. U.S. patent application Ser. No. 09/120,030, filed Jul. 21, 1998 and incorporated herein by reference. Other lysostaphin analogues, including naturally occurring enzymes of this type have been established as potent agents capable of addressing difficult to treat bacterial diseases caused by staphylococcal infection. Other peptidases with related activity are known. Thus lasA protease and achromopeptidase, reported in Kessler, et al., J. Biol. Chem. 268:7503-08 (1993) and Li et al., J. Biochem. 122:772-778(1997), respectively, have anti-staphylococcal activity based on their digestion of glycine-containing cross-links in the peptidoglycan cell wall component. These agents may be used in this invention in place of lysostaphin.

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

- **Diagnostic assay for antibiotic tolerance**

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  Patent Application Number: 20030175796

  Date filed: May 2, 2003

  Abstract: Allelic variation in the vex2, pep27 and vncS genes of bacteria responsible for tolerance to **antibiotics** such as penicillin and vancomycin, is taught. Methods for identifying **antibiotic** tolerant bacteria and subjects infected with such bacteria, particularly **antibiotic** tolerant Streptococcus pneumoniae, are provided. Test kits and components useful for performing such methods, particularly including oligonucleotide primers, are also provided.

  Excerpt(s): This invention relates to the field of diagnostics based on DNA sequence information. Antimicrobial resistance to multiple **antibiotics** is a significant and well described clinical problem; however, a less well-characterized phenomenon, antimicrobial tolerance, has emerged in pathogenic isolates of Streptococcus pneumoniae with potentially serious effects on patient outcome. Tolerance describes the ability of bacteria to stop growing in the presence of an **antibiotic,** while surviving to resume growth once the **antibiotic** is removed. Incidence of tolerance to vancomycin, the **antibiotic** of last resort for Gram-positive infections, has increased to 8% in the past few years. Tolerance has also been implicated in poor patient outcome with pneumococcal meningitis, mortality 30% versus non-tolerant 5% (unpublished data). In 1997, a locus was identified that is believed to control the activation of the major pneumococcal autolytic enzyme LytA, which is the enzyme whose loss of function is associated with tolerance. Novak, R. B. et al, "Emergence of vancomycin tolerance in Streptococcus pneumoniae`, Nature 399:590-593 (1999). The operon, vex/pep27/vncr/s, encodes for a signal peptide, Pep27, that is transported out of the cell via the Vex dedicated transporter. Novak, R. et al., "Signal transduction by a death signal peptide: uncovering the mechanism of bacterial killing by penicillin", Molec Cell. 5:49-57 (2000). Pep27 is believed to be a quorum sensing peptide. Novak et al., id. (2000). Once it reaches a critical density in the supernatant, it signals through the two-component regulatory system, VncS and VncR, which subsequently induces activation of LytA. Novak et al., id. (2000).

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

- **End selection in directed evolution**

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  Patent Application Number: 20030194763

  Date filed: March 14, 2002

  Abstract: This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of end-selection-based methods is the

ability to recover full-length polynucleotides from a library of progeny molecules generated by mutagenesis methods. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of **antibiotics,** pharmacotherapeutics, and transgenic traits.

Excerpt(s): The present application is a continuation-in-part of U.S. application Ser. No. [NOT YET ASSIGNED], filed on Feb. 4, 2000 (entitled Non-Stochastic Generation of Genetic Vaccines and Enzymes), which is hereby incorporated by reference; which is a continuation-in-part of U.S. application Ser. No. [NOT YET ASSIGNED], filed on JAN. 31, 2000 (entitled Non-Stochastic Generation of Genetic Vaccines), which is hereby incorporated by reference; which is a continuation-in-part of U.S. application Ser. No. 09/332,835 (entitled Synthetic Ligation Reassembly in Directed Evolution), which is hereby incorporated by reference; which is a continuation-in-part of U.S. application Ser. No. 09/276,860, filed on Mar. 26, 1999 (entitled Exonuclease-Mediated Gene Assembly in Directed Evolution), which is hereby incorporated by reference, which is a continuation-in-part of U.S. application Ser. No. 09/267,118, filed on Mar. 9, 1999 (entitled End Selection in Directed Evolution), which is hereby incorporated by reference, which is a continuation-in part of U.S. application Ser. No. 09/246,178, filed Feb. 4, 1999 (entitled Saturation Mutagenesis in Directed Evolution), which is hereby incorporated by reference; which is a continuation-in part of U.S. application Ser. No. 09/185,373 filed on Nov. 3, 1998 (entitled Directed Evolution of Thermophilic Enzymes), which is hereby incorporated by reference; which is a continuation of U.S. application Ser. No. 08/760,489 filed on Dec. 5, 1996 (entitled Directed Evolution of Thermophilic Enzymes, now U.S. Pat. No. 5,830,696), which is hereby incorporated by reference; which is a continuation-in-part of U.S. provisional application No. 60/008,311 filed on Dec. 07, 1995, which is hereby incorporated by reference. U.S. application Ser. No. 09/246,178, filed Feb. 4, 1999 (entitled Saturation Mutagenesis in Directed Evolution) is also a continuation-in-part of U.S. application Ser. No. 08/962,504 filed on Oct. 31, 1997 (entitled Method of DNA Shuffling), which is hereby incorporated by reference; which is a continuation-in-part of U.S. application Ser. No. 08/677,112 filed on Jul. 09, 1996 (entitled Method of DNA Shuffling with Polynucleotides Produced by Blocking or Interrupting A Synthesis or Amplification Process, now U.S. Pat. No. 5,965,408), which is hereby incorporated by reference. U.S. application Ser. No. 09/246,178, filed Feb. 4, 1999 (entitled Saturation Mutagenesis in Directed Evolution) is also a continuation-in-part of U.S. application Ser. No. 08/651,568 filed on May 22, 1996 (entitled Combinatorial Enzyme Development, now U.S. Pat. No. 5,939,250), which is hereby incorporated by reference; which is a continuation-in-part of U.S. provisional application serial No. 60/008,316, filed Dec. 7, 1995, which is hereby incorporated by reference.

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

- **Film-coated tablet for improved upper gastrointestinal tract safety**

  Inventor(s): Bekker, Petrus Jakobus; (Mason, OH), Dansereau, Richard John; (Mason, OH)

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  Patent Application Number: 20030211156

  Date filed: March 28, 2003

  Abstract: A novel oral dosage to be delivered to the stomach comprising a safe and effective amount of an active ingredient selected from the group consisting of emepronium bromidebromide, doxycycline, and other tetracyclines/antibiotics, iron preparations, quinidine, nonsteroidal anti-inflammatory drugs, alprenolol, ascorbic acid, captopril, theophylline, zidovoudine (AZT), bisphosphonates and mixtures thereof and pharmaceutically-acceptable excipients, wherein said oral dosage form is a generally oval form and film coated to facilitate rapid esophageal transit and avoid irritation in the mouth, buccal cavity, pharynx, and esophagus.

  Excerpt(s): This application claims priority under Title 35, United States code 119(e) from Provisional Application Serial No. 60/049,306 filed Jun. 11, 1997. The present invention relates to novel oral dosage forms that protect the epithelial and mucosal tissues of the mouth and the buccal cavity, the pharynx, the larynx, and the esophagus from erosion, ulceration, or other like irritation suffered by direct contact of these tissues with the active ingredient. The tablet is a modified oval shape and is film coated. This invention further relates to a method of treating or preventing diseases characterized by abnormal calcium and phosphate metabolism using the novel film coated dosage forms described herein. The oral administration of certain active ingredients sometimes results in patient complaints shortly after dosing; said complaints are usually characterized by the patients as heartburn, esophageal burning, pain and/or difficulty upon swallowing, and/or pain existing behind and/or mid-sternum. It is believed that these complaints originate from esophagitis or esophageal irritation caused by the erosion, ulceration, or other like irritation of the epithelial and mucosal tissues of the upper gastrointestinal tract, generally the mouth through the stomach, most generally the esophagus. It is hypothesized that said irritation results from the active ingredient coming in direct contact with those epithelial and mucosal tissues, resulting in the topical irritation thereof. If the dosage form adheres in the esophagus, the active ingredient slowly dissolves and creates a high drug concentration on the mucosal surface of the esophagus.

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

- **Human and mouse beta-defensins, antimicrobial peptides**

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  Patent Application Number: 20030176652

  Date filed: September 23, 2002

  Abstract: The present invention employs an iterative application of BLAST and Hidden Markov Model (HMM) based searches which identified 34.beta.-defensin genes in the human genome and 48 in the mouse genome. The present invention relates to novel antimicrobial peptides and derivatives thereof as well as the.beta.-defensin genes encoding the peptides. The invention further relates to methods of use of the peptides including a method of inhibiting microbial growth by administering an effective amount of the peptide alone or in combination with other antimicrobial agents or **antibiotics.**

  Excerpt(s): This application claims benefit of priority to U.S. Serial No. 60/323,991, filed Sep. 21, 2001, the entire contents of which is hereby incorporated by reference without reservation. This invention relates generally to antimicrobial agents and to methods of preventing microbial growth. In particular, the present invention involves compositions comprising an antimicrobial peptide and methods for its use. The first **antibiotics** were used clinically in the 1940s and 1950s, and their use has been increasing significantly since this period. Although an invaluable advance, **antibiotic** and antimicrobial therapy suffers from several problems, particularly when strains of various bacteria appear that are resistant to **antibiotics.** Interestingly, bacteria resistant to streptomycin were isolated about a year after this **antibiotic** was introduced.

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

- **Inhibitors of serine and metallo-beta-lactamases**

  Inventor(s): Buynak, John D.; (Dallas, TX), Chen, Hansong; (Dallas, TX)

  Correspondence: SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.; P.O. Box 2938; Minneapolis; MN; 55402; US

  Patent Application Number: 20030216372

  Date filed: April 4, 2003

  Abstract: Compounds of formula (I): 1wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4 and n have any of the values defined in the specification, and their pharmaceutically acceptable salts, are useful for inhibiting simultaneously serine and metallo-.beta.-lactamase enzymes, for enhancing the activity of.beta.-lactam **antibiotics,** and for treating.beta.-lactam resistant bacterial infections in a mammal. The invention also provides pharmaceutical compositions, processes for preparing compounds of formula I, and novel intermediates useful for the synthesis of compounds of formula I.

  Excerpt(s): This application claims benefit under 35 U.S.C.sctn. 119(e) of U.S. provisional application Ser. No. 60/370,499, filed Apr. 4, 2002, which application is incorporated herein by reference. The most important mechanism of microbial resistance to.beta.-lactam **antibiotics** is the bacterial production of.beta.-lactamases, enzymes that

hydrolytically destroy.beta.-lactam **antibiotics,** such as penicillins and cephalosporins. This type of resistance can be transferred horizontally by plasmids that are capable of rapidly spreading the resistance, not only to other members of the same strain, but even to other species. Due to such rapid gene transfer, a patient can become infected with different organisms, each possessing the same.beta.-lactamase.beta.-lactamase enzymes have been organized into four molecular classes: A, B, C and D based on amino acid sequence. Class A, includes RTEM and the.beta.-lactamase of Staphylococcus aureus, class C, includes the lactamase derived from P99 Enterobacter cloacae, and class D are serine hydrolases. Class A enzymes have a molecular weight of about 29 kDa and preferentially hydrolyze penicillins. The class B lactamases are metalloenzymes and have a broader substrate profile than the proteins in the other classes. Class C enzymes include the chromosomal cephalosporinases of gram-negative bacteria and have molecular weights of approximately 39 kDa. The recently recognized class D enzymes exhibit a unique substrate profile that differs significantly from the profile of both class A and class C enzymes.

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

- **Intermediate of carbapenem antibiotics and process for the preparation thereof**

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  Patent Application Number: 20030191106

  Date filed: February 10, 2003

  Abstract: There is disclosed an azetidinones compound of the formula (I): Wherein, R is hydrogen, or hydroxy protecting group, R.sub.1 and R.sub.2 are each independently alkyl of 1-15 carbon atoms, benzyl or cycloalkyl of 5-6 carbon atom which may have substituent(s), R.sub.3 is low alkyl, or low alkyl ester, R.sub.4 is aryl, or aryl substituted with halogen, alkoxy of 1-6 carbon atom, nitro groups which is useful as a synthetic intermediate of the 1'.beta.-methylcarbapenem-type antibacterial agent.

  Excerpt(s): wherein, R is a hydrogen atom or a protecting group of hydroxy; R.sub.1 and R.sub.2 are independently C.sub.1-C.sub.15 alkyl, benzyl or cyclized to be 5 or 6-membered ring which is cyclic hydrocarbon or heterocyclic compound containing at least one of O and S; R.sub.3 is a lower alkyl or a lower alkyl ester; R.sub.4 is benzene or benzene substituted with halogen atom, a lower alkoxy or nitro; and, the methyl group in 1' position is R configuration, which is expressed by.beta.-methyl in all general formula hereunder. wherein R, R.sub.1, R.sub.2, R.sub.3 and R.sub.4 are the same as defined above; and, X is a halogen atom. Further, this invention relates to.alpha.-halopropionamide compound of the general formula (III), a novel stereoselective additive.

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

- **Local delivery of long lasting therapeutic agents**

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  Patent Application Number: 20030170250

  Date filed: May 20, 2002

  Abstract: Methods of and compositions for localized delivery of therapeutic agents which are capable of forming covalent bonds with a site of interest are disclosed. Therapeutic agents useful in the invention include wound healing agents, **antibiotics,** anti-inflammatories, anti-oxidants, anti-proliferatives, immunosupressants, anti-infective and anti-cancer agents.

  Excerpt(s): This invention relates to the field of therapeutic agents in medicine. In particular, this invention relates to the field of localized delivery of therapeutic agents wherein the agents are capable of covalently bonding to a site of interest in vivo, to provide increased tissue retention and pharmacodynamic duration of therapeutic benefit for the given drug. The technology of local delivery of a therapeutic using drug delivery catheters or devices is well established. Under ideal circumstances, the therapeutic agent will remain near the site of administration for increased effectiveness. While useful, the main drawback of this technology is the rate at which the therapeutic agent is washed away from the site of application. For example, according to Imanishi et al. (J Cardio, 1996, 27, 267-271), the concentration of residual argatroban introduced through pressure balloon catheter is decreased by three folds in the first five minutes after deflation of the balloon. This phenomenon is reported repeatedly in the literature for other therapeutic agents resulting in a general deficiency that drugs from a diverse therapeutic areas have limited utility following localized delivery due to their inability to maintain adequate concentrations within hours after delivery (Circulation, 1994, 89 (4), 1518-1524; Circulation, 1997, 96 (1), 154-165). As a result, repeated dosings of locally administered therapeutic agents are required in order to avoid rapid reduction of drug levels and sub-optimal performance or sub-effective responsiveness. This results in increased costs and unnecessary patient exposure to excessive amounts of therapeutic agents. Thus, there is a need to provide therapeutic agents to localized sites such that the therapeutic agents have increased retention at the desired site and prolonged duration of action. These therapeutic agents are not as easily washed away from the site of administration so that reduced amounts of the agents can be supplied. In particular, there is a need to provide therapeutic agents capable of forming covalent bonds to localized sites such that the therapeutic agents have increased effective presence for therapeutic benefits.

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

- **Macrolide antiinfective agents**

  Inventor(s): Chu, Daniel T. W.; (Santa Clara, CA)

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  Patent Application Number: 20030207821

  Date filed: February 3, 2003

Abstract: The invention is directed towards antibacterial compounds. The invention concerns macrolide **antibiotics** useful as antiinfective agents.

Excerpt(s): This application claims priority under 35 U.S.C.sctn. 119 from U.S. provisional patent application Serial Nos. 60/173,805 filed Dec. 30, 1999, and 60/173,804 filed Dec. 30, 1999 and U.S. utility patent application Ser. Nos. 09/551,162 filed Apr. 14, 2000, which in turn claims priority from U.S. provisional patent application Serial Nos. 60/129,729 filed Apr. 16, 1999 and 60/172,154 filed Dec. 17, 1999, and Ser. No. 09/550,045 filed Apr. 14, 2000, which in turn claims priority from U.S. provisional patent application Serial Nos. 60/140,175 filed Jun. 18, 1999 and 60/172,159 filed Dec. 17, 1999. The contents of these provisional and utility applications are relied on and incorporated herein in their entirety by reference. The invention is directed to antibacterial compounds that expand the repertoire of erythromycin-like **antibiotics.** More particularly, the invention concerns macrolide **antibiotics** containing an erythronolide nucleus modified at least at the substituent at C-13. The increasing number of microbial strains that have acquired resistance to the currently available known **antibiotic** compounds is recognized as a dangerous threat to public health. As the use of such compounds has proliferated, so too has the need for expanding the options available to treat a wide variety of microbial-based conditions. The need for a larger choice of antimicrobial compounds extends beyond treatment of human infection and to a need to preserve food and other perishable commodities. New **antibiotics** can also be essential for resistant plants and animals as well as to provide resistance to materials that otherwise are subject to microbially caused corrosion.

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

- **Macrolides with antibacterial activity**

Inventor(s): Angehrn, Peter; (Boeckten, CH), Hunziker, Daniel; (Moehlin, CH), Wyss, Pierre-Charles; (Therwil, CH)

Correspondence: HOFFMANN-LA ROCHE INC.; PATENT LAW DEPARTMENT; 340 KINGSLAND STREET; NUTLEY; NJ; 07110

Patent Application Number: 20030199459

Date filed: February 21, 2003

Abstract: The invention provides new macrolides **antibiotics** of formula (I) with improved biological properties and improved stability formula (I): wherein R.sup.1 is hydrogen, cyano, --S(L).sub.mR.sup.2, --S(O)(L).sub.mR.sup.2, or --S(O).sub.2(L).sub.mR.sup.2; L represents --(CH.sub.2).sub.n-- or --(CH.sub.2).sub.nZ(CH.sub.2).sub.n'---; m is 0 or 1; n is 1, 2, 3, or 4; n' is 0, 1, 2, 3, or 4; Z is O, S or NH; R2 is hydrogen, alkyl, heterocyclyl or aryl; which heterocyclyl and the aryl groups may be further substituted; * indicates a chiral center which is in the (R) or (S) form and pharmaceutically acceptable acid addition salts or in vivo cleavable esters thereof. 1

Excerpt(s): This invention relates to new macrolide **antibiotics** with improved activity and stability, to the use of such **antibiotics** for the treatment of infectious diseases and to compositions containing such macrolides. Many different semisynthetic third generation derivatives of the ketolide class of macrolide **antibiotics** have been described, the most potent being HMR 3647 or telithromycin (4) (EP 680967 A1 (1995); FR 2732684 A1 (1996); Bioorg. Med. Chem. Lett. (1999), 9(21), 3075-3080.) and ABT 773 (WO 9809978 (1998); J. Med. Chem. 2000, 43, 1045). However, none of these agents

described thus far have been able to overcome constitutive MLS B resistance in Staphylococcus aureus. * indicates a chiral center which is in the (R) or (S) form.

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

- **Method and apparatus for preparing biomimetic scaffold**

  Inventor(s): Campbell, Phil G.; (Pittsburgh, PA), Weiss, Lee E.; (Pittsburgh, PA)

  Correspondence: FOLEY HOAG, LLP; PATENT GROUP, WORLD TRADE CENTER WEST; 155 SEAPORT BLVD; BOSTON; MA; 02110; US

  Patent Application Number: 20030175410

  Date filed: March 18, 2003

  Abstract: Methods, compositions, and apparatus for preparing biomimetic scaffolds are provided. The methods, compositions, and apparatus are compatible with both in situ and external scaffold preparation. Also provided are methods for preparing scaffolds having 3-D spatial and/or temporal gradients of therapeutic compounds, such as, growth factors, **antibiotics,** immunosuppressants, analgesics, etc.

  Excerpt(s): This application claims the benefit of Provisional Patent Application No. 60/365,451 filed Mar. 18, 2002 which is hereby incorporated by reference in its entirety. Clinical use of grafts of living tissue have recently moved from direct implantation of freshly harvested fully formed tissue, e.g. skin grafts or organ transplants, to strategies involving seeding of cells and signaling molecules on matrices which will regenerate or encourage the regeneration of local structures. For certain tissues it may be desirable to provide mechanical support of the existing structure by replacement or substitution of the tissue for at least some of the healing period. Thus, a device or scaffold having a specific architecture may be used to encourage the migration, residence and proliferation of specific cell types as well as provide mechanical and structural support during healing. In order to encourage cellular attachment and growth, the overall porosity of the device is important. Additionally, the individual pore diameter or size is an important factor in determining the ability of cells to migrate into, colonize, and differentiate while in the device (Martin, R B et al. Biomaterials, 14: 341, 1993). For skeletal tissues, bone and cartilage, guided support to reproduce the correct geometry and shape of the tissue is thought to be important. It is generally agreed that pore sizes of above 150.mu.m and preferably larger (Hulbert, et al., 1970; Klawitter, J. J, 1970; Piecuch, 1982; and Dennis, et al., 1992) and porosity greater than 50% are necessary for cell invasion of the carrier by bone forming cells. It has been further accepted that a tissue regenerating scaffold must be highly porous, greater than 50% and more preferably more than 90%, in order to facilitate cartilage formation.

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

- **METHODS FOR IDENTIFYING AGENTS THAT INTERACT WITH AN ACTIVE SITE**

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  Patent Application Number: 20030211588

  Date filed: January 25, 2001

  Abstract: This invention is directed to the crystal structure of Acyl Carrier Protein Synthase (ACPS) complexed with Acyl Carrier Protein (ACP), the solution structure of B. subtilis ACP, and to the use of these structures in rational drug design methods to identify agents that may interact with active sites of ACPS and ACP, and to the testing of these agents to identify agents that may represent novel **antibiotics.**

  Excerpt(s): This application claims the benefit of U.S. Provisional Application No. 60/202,466 filed May 8, 2000. The present invention relates to the crystal structure of the ACPS/ACP complex, as well as the three-dimensional solution structure of B. subtilis ACP. These structures are critical for the design and selection of potent and selective agents which interact with ACPS and ACP, and particularly, the design of novel **antibiotics.** Acyl Carrier Proteins (ACPs) play important roles in a number of biosynthetic pathways that are dependent upon acyl group transfers [1]. They are most often associated with the biosynthesis of fatty acids [2,3], but they are also utilized in the synthesis of polyketide **antibiotics** [4,5], non-ribosomal peptides [6,7], and of intermediates used in the synthesis of vitamins such as the protein-bound coenzymes, lipoic acid [8] and biotin [9]. The ACP in each of these pathways is composed of 80-100 residues and is either an integrated domain in a larger multi-functional protein (Type I synthase complex) or is a structurally independent protein that is part of a non-aggregated multi-enzyme system (Type II synthase complex). Type I synthases are found in mammals, fungi and certain Mycobacteria while type II ACPs are utilized by plants and most bacteria. The Escherichia coli ACP for fatty acid synthesis has been over-expressed [10] and purified [11,12], and the solution structure has been solved by NMR spectroscopy [13]. The fact that these proteins are essential for the maturation of the organism has led to their investigation as targets for the development of new anti-microbial agents [14-18].

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

- **Methods for identifying pathway-specific reporters and target genes, and uses thereof**

  Inventor(s): Roberts, Christopher J.; (Seattle, WA)

  Correspondence: PENNIE AND EDMONDS; 1155 AVENUE OF THE AMERICAS; NEW YORK; NY; 100362711

  Patent Application Number: 20030211475

  Date filed: September 5, 2001

  Excerpt(s): The present invention relates to methods for identifying one or more reporter genes for a particular biological pathway of interest. The reporter genes of this invention

are particularly useful for analyzing the activity of particular biological pathways of interest, and may be further used in the design of drugs, drug therapies or other biological agents (e.g., insecticides, herbicides, fungicides, **antibiotics,** or antivirals) to target a particular biological pathway. The present invention also relates to methods for identifying one or more target genes for a particular biological pathway of interest. Target genes of the invention are useful as specific targets for drug which may be designed to enhance, inhibit, or modulate a particular biological pathway. Methods to identify gene which modifies the function or structure of a member (e.g., compound or gene product) of a particular biological pathway are provided. The present invention provides examples of reporter genes and/or target genes which have been discovered by the methods of the invention. Specifically, the inventors have made the surprising discovery that five S. cerevisiae genes (previously of unknown function) form clustered co-regulated sets of genes and are reporters of the ergosterol-pathway. The methods of the invention are also exemplified in that the inventors have specifically discovered six S. cerevisiae reporter genes of the protein kinase C (PKC) pathway. Two of these genes are also novel target genes of the PKC pathway and provide targets for the development of PKC pathway-specific drugs, drug therapies, or other related biological or therapeutical agents. The methods of the invention are further exemplified by the discovery of four novel reporter genes of the S. cerevisiae Invasive Growth pathway. One of these genes also serves as a target gene in the Invasive Growth pathway, and may be used to develop Invasive Growth pathway-specific drugs, drug therapies, or other related biological or therapeutical agents. Citation of a reference herein shall not be construed as an admission that such reference is prior art to the present invention.

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

- **Methods for production of p-hydroxybenzoate in bacteria**

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  Patent Application Number: 20030158397

  Date filed: October 1, 2001

  Abstract: This invention relates to the isolation of a novel tonB operon from Pseudomonas putida. These genes are useful to render the cells more sensitive to **antibiotics,** toluene, pHBA, aromatic compounds, parabenes, and aromatic amino acids after inactivation with specific mutant allels or more tolerant to these compounds after overexpression with appropriate expression vector. These findings are important in the field of medicine and biotechnology and biocatalysis. In addition a screen to identify pHBA tolerant genes is provided and strains with significant tolerance to pHBA were identified. These strains are important for pHBA production.

  Excerpt(s): The present invention relates to the fields of molecular biology and microbiology. More specifically, this invention pertains to a novel gene cluster, tonB operon (exbB, exbD, tonB) and its role in tolerance to aromatic compounds, aromatic amino acids, p-hydroxybenzoic acid (pHBA), and bactericidal agents in bacteria. In addition, a method for screening and characterizing pHBA tolerance is provided. By these methods, some strains with particular tolerance to pHBA were identified. Also provided are methods for producing bacterial strains which are more sensitive or

tolerant to a variety of chemical compounds. Toxicity of aromatic compounds, **antibiotics,** organic solvents and bacteriocidic agents to microorganisms presents a major problem in the field of microbiology. In addition, tolerance to pHBA, **antibiotics,** aromatic compounds, parabenes and aromatic amino acids are of significant importance in various biotechnology areas such as biotransformation, biodegradation, food, pharmaceuticals, and cosmetics. Factors influencing tolerance appear to be varied and not always understood. Increasingly, attention has turned to genetic manipulation to create microbes that are able to thrive in high concentrations of aromatic compounds and organic solvents or to create microbes that are more sensitive to **antibiotics** and bacteriocidic agents, e.g., parabene preservatives. Among these are microbes that can synthesize monomers that can be used for the ulterior synthesis of added value polymers. One of these products of interest is pHBA that can be synthesized from toluene as described below. para-Hydroxybenzoic acid (pHBA) is a key monomer for production of liquid crystal polymers, (e.g., Zenite.RTM. that are used in board displays of computers and other electronic devices and for parabene preservatives). A current limitation on the biotransformation of toluene into pHBA is the relative toxicity of these compounds for cells (Sikema et al., Microbiol. Rev. 50:201-222 (1995), as well as the toxicity of the product being produced (WO 9856920). One enzymatic pathway of increasing commercial interest for biotransformation is that of toluene degradation through the toluene monooxygenase pathway (TMO pathway). This pathway includes the following steps: toluene is oxidized to p-cresol with toluene monooxygenase, p-cresol is progressively oxidized to p-hydroxybenzyl alcohol and p-hydroxybenzaldehyde with p-cresol methylhydroxylase, and p-hydroxybenzaldehyde is then oxidized to p-hydroxybenzoic acid (pHBA) with p-hydroxybenzaldehyde dehydrogenase and pHBA is further oxidized to protocatechuic acid (PCA) with p-hydroxybenzoate hydroxylase. PCA is further metabolized to the TCA cycle where it is used for cell biosynthesis or energy metabolism.

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

- **METHODS FOR THE IDENTIFICATION OF INHIBITORS OF HOMOCITRATE SYNTHASE AS ANTIBIOTICS**

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  Patent Application Number: 20030180829

  Date filed: November 9, 2001

  Abstract: The present inventors have discovered that homocitrate synthase is essential for fungal pathogenicity. Specifically, the inhibition of homocitrate synthase gene expression in fungi results in no signs of successful infection or lesions. Thus, homocitrate synthase can be used as a target for the identification of **antibiotics,** preferably antifungals. Accordingly, the present invention provides methods for the identification of compounds that inhibit homocitrate synthase expression or activity.

The methods of the invention are useful for the identification of **antibiotics,** preferably antifungals.

Excerpt(s): The invention relates generally to methods for the identification of **antibiotics,** preferably antifungals that affect the biosynthesis of lysine. This application is co-pending with our application entitled "Methods for the Identification of Inhibitors of.alpha.-Aminoadipate Reductase as Antibiotics". Filamentous fungi are the causal agents responsible for many serious pathogenic infections of plants and animals. Since fungi are eukaryotes, and thus more similar to their host organisms than, for example bacteria, the treatment of infections by fungi poses special risks and challenges not encountered with other types of infections. One such fungus is Magnaporthe grisea, the fungus that causes rice blast disease. It is an organism that poses a significant threat to food supplies worldwide. Other examples of plant pathogens of economic importance include the pathogens in the genera Agaricus, Alternaria, Anisogramma, Anthracoidea, Antrodia, Apiognomonia, Apiosporina, Armillaria, Ascochyta, Aspergillus, Bipolaris, Bjerkandera, Botryosphaeria, Botrytis, Ceratobasidium, Ceratocystis, Cercospora, Cercosporidium, Cerotelium, Cerrena, Chondrostereum, Chryphonectria, Chrysomyxa, Cladosporium, Claviceps, Cochliobolus, Coleosporium, Colletotrichium, Colletotrichum, Corticium, Corynespora, Cronartium, Cryphonectria, Cryptosphaeria, Cyathus, Cymadothea, Cytospora, Daedaleopsis, Diaporthe, Didymella, Diplocarpon, Diplodia, Discohainesia, Discula, Dothistroma, Drechslera, Echinodontium, Elsinoe, Endocronartium, Endothia, Entyloma, Epichloe, Erysiphe, Exobasidium, Exserohilum, Fomes, Fomitopsis, Fusarium, Gaeumannomyces, Ganoderma, Gibberella, Gloeocercospora, Gloeophyllum, Gloeoporus, Glomerella, Gnomoniella, Guignardia, Gymnosporangium, Helminthosporium, Herpotrichia, Heterobasidion, Hirschioporus, Hypodermella, Inonotus, Irpex, Kabatiella, Kabatina, Laetiporus, Laetisaria, Lasiodiplodia, Laxitextum, Leptographium, Leptosphaeria, Leptosphaerulina, Leucytospora, Linospora, Lophodermella, Lophodermium, Macrophomina, Magnaporthe, Marssonina, Melampsora, Melampsorella, Meria, Microdochium, Microsphaera, Monilinia, Monochaetia, Morchella, Mycosphaerella, Myrothecium, Nectria, Nigrospora, Ophiosphaerella, Ophiostoma, Penicillium, Perenniporia, Peridermium, Pestalotia, Phaeocryptopus, Phaeolus, Phakopsora, Phellinus, Phialophora, Phoma, Phomopsis, Phragmidium, Phyllachora, Phyllactinia, Phyllosticta, Phymatotrichopsis, Pleospora, Podosphaera, Pseudopeziza, Pseudoseptoria, Puccinia, Pucciniastrum, Pyricularia, Rhabdocline, Rhizoctonia, Rhizopus, Rhizosphaera, Rhynchosporium, Rhytisma, Schizophyllum, Schizopora, Scirrhia, Sclerotinia, Sclerotium, Scytinostroma, Septoria, Setosphaera, Sirococcus, Spaerotheca, Sphaeropsis, Sphaerotheca, Sporisorium, Stagonospora, Stemphylium, Stenocarpella, Stereum, Taphrina, Thielaviopsis, Tilletia, Trametes, Tranzschelia, Trichoderma, Tubakia, Typhula, Uncinula, Urocystis, Uromyces, Ustilago, Valsa, Venturia, Verticillium, Xylaria, and others. Related organisms in the classification, oomycetes, that include the genera Albugo, Aphanomyces, Bremia, Peronospora, Phytophthora, Plasmodiophora, Plasmopara, Pseudoperonospora, Pythium, Sclerophthora, and others are also significant plant pathogens and are sometimes classified along with the true fungi. Human diseases that are caused by filamentous fungi include life-threatening lung and disseminated diseases, often a result of infections by Aspergillus fumigatus. Other fungal diseases in animals are caused by fungi in the genera, Fusarium, Blastomyces, Microsporum, Trichophyton, Epidermophyton, Candida, Histoplamsa, Pneumocystis, Cryptococcus, other Aspergilli, and others. The control of fungal diseases in plants and animals is usually mediated by chemicals that inhibit the growth, proliferation, and/or pathogenicity of the fungal organisms. To date, there are less than twenty known modes-of-action for plant protection fungicides and human antifungal compounds. A

pathogenic organism has been defined as an organism that causes, or is capable of causing disease. Pathogenic organisms propagate on or in tissues and may obtain nutrients and other essential materials from their hosts. A substantial amount of work concerning filamentous fungal pathogens has been performed with the human pathogen, Aspergillus fumigatus. Shibuya et al. (Shibuya, K., M. Takaoka, et. al. (1999) Microb Pathog 27: 123-31 (PMID: 10455003)) have shown that the deletion of either of two suspected pathogenicity related genes encoding an alkaline protease or a hydrophobin (rodlet) respectively, did not reduce mortality of mice infected with these mutant strains. Smith et al. (Smith, J. M., C. M. Tang, et al. (1994) Infect Immun 62: 5247-54 (PMID: 7960101)) showed similar results with alkaline protease and the ribotoxin restrictocin; Aspergillus fumigatus strains mutated for either of these genes were fully pathogenic to mice. Reichard et al. (Reichard, U., M. Monod, et al. (1997) J Med Vet Mycol 35: 189-96 (PMID: 9229335)) showed that deletion of the suspected pathogenicity gene encoding, aspergillopepsin (PEP) in Aspergillus fumigatus, had no effect on mortality in a guinea pig model system, and Aufauvre-Brown et al (Aufauvre-Brown, A., E. Mellado, et al. (1997) Fungal Genet Biol 21: 141-52 (PMID: 9073488)) showed no effects of a chitin synthase mutation on pathogenicity. However, not all experiments produced negative results. Ergosterol is an important membrane component found in fungal organisms. Pathogenic fungi that lack key enzymes in this biochemical pathway might be expected to be non-pathogenic since neither the plant nor animal hosts contain this particular sterol. Many antifungal compounds that affect this biochemical pathway have been described (Onishi, J. C. and A. A. Patchett (1990 a, b, c, d, and e) U.S. Pat. Nos. 4,920,109; 4,920,111; 4,920,112; 4,920,113; and 4,921,844, Merck & Co. Inc. (Rahway N.J.)) and (Hewitt, H. G. (1998) Fungicides in Crop Protection Cambridge, University Press). D'Enfert et al. (D'Enfert, C., M. Diaquin, et al. (1996) Infect Immun 64: 4401-5 (PMID: 8926121)) showed that an Aspergillus fumigatus strain mutated in an orotidine 5'-phosphate decarboxylase gene was entirely non-pathogenic in mice, and Brown et al. (Brown, J. S., A. Aufauvre-Brown, et al. (2000) Mol Microbiol 36:1371-80 (PMID: 10931287)) observed a non-pathogenic result when genes involved in the synthesis of para-aminobenzoic acid were mutated. Some specific target genes have been described as having utility for the screening of inhibitors of plant pathogenic fungi. Bacot et al. (Bacot, K. O., D. B. Jordan, et al. (2000) U.S. Pat. No. 6,074,830, E. I. du Pont de Nemours & Company (Wilmington Del.)) describe the use of 3,4-dihydroxy-2-butanone 4-phosphate synthase, and Davis et al. (Davis, G. E., G. D. Gustafson, et al. (1999) U.S. Pat. No. 5,976,848, Dow AgroSciences LLC (Indianapolis Ind.)) describe the use of dihydroorotate dehydrogenase for potential screening purposes.

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

- **Methods of disease treatment using metal-complexed tetracycline antibiotics**

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  Patent Application Number: 20030171340

  Date filed: February 5, 2003

  Abstract: A method for treating bacterial diseases, including bacterial infections, that are otherwise resistant to **antibiotics,** such as tetracycline and related compounds, using metal-complexed **antibiotics** is disclosed. Also disclosed is a method for protecting

against such diseases. The metal-complexed **antibiotics** include tetracyclines complexed with metals such as iron, copper and calcium.

Excerpt(s): This application claims priority of U.S. Provisional Application Serial No. 60/355,560, filed Feb. 7, 2002, the disclosure of which is hereby incorporated by reference in its entirety. This invention relates to a method of treating **antibiotic,** especially cycline and quinolone **antibiotic,** resistant bacterial infections using metal complexed cyclic **antibiotics,** such as metal-complexed tetracycline. A wide variety of **antibiotics** have been used to combat bacterial infection while the development of **antibiotic** resistance continues to increase. The latter problem has been largely the result of both misuse and overuse of **antibiotics** and therapeutic agents, which serves to select for microorganisms carrying the relatively rare trait(s) providing resistance to these same **antibiotics.** This selection method results in a higher frequency of the traits providing resistance and a population of **antibiotic** resistant microorganisms. Most resistance determinants can be transferred to other bacteria via plasmids and transposons exchanged by cell-cell contact, by free naked DNA from lysed cells, and by bacteriophages. This capacity for genetic transfer, coupled with the selective ability of **antibiotics** results in the presence of common genes in diverse microorganisms from different ecological and geographical niches. In sum, **antibiotics** select for the survivors which then thwart their efficacy. (see: Levy et al, 1999).

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

- **Microbiological control in poultry processing**

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  Patent Application Number: 20030211210

  Date filed: December 6, 2002

  Abstract: A method of controlling microbial contamination of poultry carcasses in the processing of poultry as food products is described. The method comprises contacting the carcasses with an aqueous medium containing an effective microbial inhibiting amount of active bromine resulting from the addition to the medium of (i) at least one 1,3-dibromo-5,5-dialkylhyd- antoinin which one of the alkyl groups is a methyl group and the other alkyl group contains in the range of 1 to about 4 carbon atoms or (ii) a solution thereof, or (iii) both of (i) and (ii). Such contacting inhibits contamination of the carcasses by microorganisms, even at least some bacteria that are resistant to **antibiotics** or antibacterials. Also described are improvements in a poultry chill tank containing an aqueous medium and a plurality of poultry carcasses in contact with the medium. Such improvements result from the presence in the medium of an effective microbial inhibiting amount of active bromine in the medium, which amount results from the addition to water before it enters the tank or while it is in the tank, or both, of (i) at least one of the above 1,3-dibromo-5,5-dialkylhydantoins, and/or a solution thereof.

  Excerpt(s): This is a continuation-in-part of commonly-owned copending application Ser. No. 10/029,329, filed Dec. 21, 2001, which in turn is a continuation-in-part of commonly-owned copending application Ser. No. 09/893,581, filed Jun. 28, 2001. Reference is hereby made to the following commonly-owned applications: application Ser. No. 09/088,300, filed Jun. 1, 1998, now U.S. Pat. No. 6,068,861 issued May 30, 2000; application Ser. No. 09/296,499, filed Apr. 22, 1999, now U.S. Pat. No. 6,110,387 issued

Aug. 29, 2000; application Ser. No. 09/323,348, filed Jun. 1, 1999, now U.S. Pat. No. 6,303,038 B1 issued Oct. 16, 2001; application Ser. No. 09/404,184, filed Sep. 24, 1999; application Ser. No. 09/442,025, filed Nov. 17, 1999, now U.S. Pat. No. 6,306,441 issued Oct. 23, 2001; application Ser. No. 09/451,319, filed Nov. 30, 1999; application Ser. No. 09/451,344, filed Nov. 30, 1999; application Ser. No. 09/456,781, filed Dec. 8, 1999; application Ser. No. 09/483,896, filed Jan. 18, 2000, application Ser. No. 09/484,687, filed Jan. 18, 2000, application Ser. No. 09/484,844, filed Jan. 18, 2000; application Ser. No. 09/484,891, filed Jan. 18, 2000; application Ser. No. 09/484,938, filed Jan. 18, 2000; application Ser. No. 09/487,816, filed Jan. 18, 2000; application Ser. No. 09/506,911, filed Feb. 18, 2000; application Ser. No. 09/658,839, filed Sep. 8, 2000; application Ser. No. 09/663,788, filed Sep. 18, 2000; application Ser. No. 09/663,948, filed Sep. 18, 2000, now U.S. Pat. No. 6,299,909 B1 issued Oct. 9, 2001; application Ser. No. 09/732,601, filed Dec. 7, 2000; application Ser. No. 09/775,516, filed Feb. 2, 2001; application Ser. No. 09/778,228, filed Feb. 6, 2001; application Ser. No. 09/785,890, filed Feb. 16, 2001; application Ser. No. 09/893,581, filed Jun. 28, 2001; and application Ser. No. 09/974,622, filed Oct. 9, 2001. Reference is also hereby made to application Ser. No. 10/028,631, filed Dec. 21, 2001, entitled "Microbiological Control in Animal Processing".

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

- **Microsphaeropsin B as novel antibacterial agent, process for producing the same and pharmaceutical composition containing thereof**

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  Patent Application Number: 20030166707

  Date filed: October 17, 2002

  Abstract: One of the aspects of the present invention is directed to tetramic acid derivatives useful in treating or preventing bacterial diseases, especially diseases caused by gram-positive pathogens resistant to **antibiotics** of the prior art. Within the scope of the present invention are pharmaceutical compositions containing at least one of the tetramic acid derivatives of the invention as the active ingredient, methods of treating and/or preventing a bacterial disease by administering at least one of the tetramic acid derivatives of the invention, and the use of the tetramic acid derivatives of the invention in the treatment and/or prevention of a bacterial disease. Preferably, the tetramic acid derivative of the invention is a compound of formula IV shown below. 1

  Excerpt(s): This application claims the benefit of U.S. Provisional Patent Application, No. 60/329,537, filed Oct. 17, 2001, the disclosure of which is incorporated by reference. The present invention relates to tetramic acid derivatives, in particular Microsphaeropsin B, as **antibiotics** having antibacterial activities, especially against Gram positive pathogens including Vancomycin resistant Enterococcus faecalis (VRE), a process for the production thereof and a pharmaceutical composition containing at least one of the tetramic acid derivatives. Bacteria are very adaptable microorganisms that possess the ability to adapt and to survive under adverse conditions. Doctors in hospitals and clinics around the world are losing the battle against an onslaught of new

drug resistant bacterial infections including those caused by Staphylococci, Streptococci, Enterococci and Pseudomonas.

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

- **Multivalent macrolide antibiotics**

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  Patent Application Number: 20030176670

  Date filed: December 27, 2002

  Abstract: Disclosed are multibinding compounds which include macrolide **antibiotics,** aminoglycosides, lincosamides, oxazolidinones, streptoramins, tetracycline and/or other compounds which bind to bacterial ribosomal RNA and/or to one or more proteins involved in ribosomal protein synthesis in the bacterium, which are useful in treating bacterial infections. The compounds adversely affect protein expression and have an antibacterial effect. The multibinding compounds of this invention containing from 2 to 10 ligands covalently attached to one or more linkers. Each ligand is macrolide **antibiotic,** aminoglycoside, lincosamide, oxazolidinone, streptogramin, tetracycline or other compound which binds to bacterial ribosomal RNA and/or one or more proteins involved in ribosomal protein synthesis in the bacterium.

  Excerpt(s): This application claims the benefit of U.S. Provisional Patent Application Serial Nos. 60/088,448 filed Jun. 8, 1998 and 60/093,072 filed Jul. 16, 1998 both of which are incorporated herein by reference in their entirety. This invention relates to novel multibinding compounds (agents) that are macrolide **antibiotics,** aminoglycosides, lincosamides, oxazolidinones, streptogramins, tetracyclines or other compounds which bind to bacterial ribosomal RNA or one or more proteins involved in ribosomal protein synthesis in the bacterium, and to pharmaceutical compositions comprising such compounds. The compounds are useful as antibacterial agents for treating a variety of bacterial infections. Organisms generate polypeptides (proteins) in order to survive. Organisms that cannot generate proteins cannot maintain viability. Because the majority of genes encode proteins, "gene expression" is nearly synonymous with protein synthesis. Gene expression involves two steps--transcription and translation. Genes code for proteins using various codons (units of three nucleotides), such as start codons (which initiate translation), stop codons (which stop translation) and codons in between the start and stop codons which selectively code for the various amino acids.

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

- **Neurotherapeutic composition and method therefor**

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  Patent Application Number: 20030158172

  Date filed: August 20, 2002

Abstract: Neurotherapeutically pharmaceutical effective compositions are prepared using carboxypeptidase E inhibitors. One class of carboxypeptidase E inhibitors found to exhibit significant neurotropic activity are.beta.-lactam compounds, particularly penam and cephem.beta.-lactam **antibiotics** and non-antibiotic derivatives thereof.

Excerpt(s): This application is a continuation of U.S. patent application No. 09/783,201, filed Feb. 14, 2001, which is expressly incorporated by reference herein. This invention relates to a novel mechanism of neuropsychiatric intervention. More particularly, this invention is directed to pharmaceutical formulations and methods for treatment of a variety of neurological disease states, including cognitive and behavioral disorders. The pharmaceutical industry has directed extensive research and development efforts toward discovery and commercialization of drugs for treatment of neurological disorders. Such disorders typically derive from chemical imbalances in the brain. Overproduction or underproduction of pertinent neurochemical species and/or receptor dysfunction has been identified with many disease states recognized by neurologists, psychiatrists, psychologists and other medical practitioners skilled in the diagnosis and treatment of mental disease. Most of the discovery effort for new neurologically active drugs has been based on the study of agonist/antagonist drug interaction with one or more of the numerous receptors in the brain and/or their respective receptor ligands.

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

- **Novel endophytic fungi and methods of use**

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Patent Application Number: 20030186425

Date filed: April 11, 2002

Abstract: This invention provides a novel endophytic fungus, Muscodor, that produces a mixture of volatile **antibiotics** with activity on specific plant pathogens, bacteria, nematodes and insects. Also provided is a method for treating or protecting plants, soil and seeds from microbial infections comprising applying an effective amount of a volatile **antibiotic** producing Muscodor sp. The invention also relates to fungicidal, bactericidal, insecticidal and nematicidal compositions comprising this novel Muscodor strain and the **antibiotics** and metabolites produced by this strain either alone, or in combination with other chemical and biological pesticides. Also provided is a method for identifying and isolating related gas producing fungi.

Excerpt(s): This application claims the benefit under 35 U.S.C.sctn. 119(e) of U.S. Provisional Application Nos. 60/283,902 and 60/363,072, filed Apr. 16, 2001 and Mar. 11, 2002, respectively. The contents of these applications are hereby incorporated by reference into the present disclosure. The present invention relates to the isolation of novel fungi that produce volatile **antibiotics.** The volatile compounds have biological activity against plant and human pathogenic fungi and bacteria, insects and nematodes. Throughout this application, various articles and books are referenced by authorship and date. The fall bibliographic citation for each publication can be found at the end of the specification, immediately preceding the claims.

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

- **Novel substituted succinic acid metallo-beta-lactamase inhibitors and their use in treating bacterial infections**

  Inventor(s): Balkovec, James M.; (Martinsville, NJ), Greenlee, Mark L.; (Rahway, NJ), Olson, Steven H.; (Metuchen, NJ), Rouen, Gregory P.; (New Brunswick, NJ)

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  Patent Application Number: 20030207859

  Date filed: January 9, 2003

  Abstract: This invention relates to novel substituted succinic acid metallo-.beta.-lactamase inhibitors which are useful potentiators of.beta.-lactam **antibiotics.** Accordingly, the present invention provides a method of treating bacterial infections in animals or humans which comprises administering, together with a b-lactam **antibiotic,** a therapeutically effective amount of a compound of formula I: 1including pharmaceutically acceptable salts, prodrugs, anhydrides, and solvates thereof.

  Excerpt(s): The present invention relates to compounds which have metallo-.beta.-lactamase inhibitory characteristics. The invention also relates to methods of preparing, pharmaceutical compositions and uses of the compounds. Metallo-.beta.-lactamases are bacterial enzymes which confer resistance to virtually all clinically relevant.beta.-lactam **antibiotics,** including carbapenems and jeopardize the future use of all such agents. The increased treatment of infections with carbapenems and other.beta.-lactam **antibiotics** may lead to the proliferation of clinical bacterial strains which are able to produce metallo-.beta.-lactamases and thus resist the effects of.beta.-lactam **antibiotics.** In fact, metallo-.beta.-lactamases have now been identified in a number of pathogenic bacterial species including Bacillus cereus, Bacteroides fragilis, Aeromonas hydrophila, Klebsiella pneumoniae, Pseudomonas aeruginosa, Serratia marcescens, Stenotrophomonas maltophilia, Shigella flexneri, Legionella gormanii, Chryseobacterium meningosepticum, Chryseobacterium indologenes, Acinetobacter baumannii, Citrobacter freundii, and Aeromonas veronii. Accordingly, there is an increasing need for agents which when combined with a.beta.-lactam **antibiotic,** e.g. imipenem, will restore the effectiveness of the.beta.-lactam **antibiotics** and which are at the same time relatively free from undesirable side effects.

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

- **Ophthalmic sulcus speculum**

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  Correspondence: Robert W. Fieseler; McAndrews, Held & Malloy, Ltd.; 34th Floor; 500 West Madison Street; Chicago; IL; 60661; US

  Patent Application Number: 20030171656

  Date filed: January 21, 2003

  Abstract: Devices in accordance with certain embodiments of the present sulcus speculum are designed to be placed into the sulcus of an eye to perform one or more of the following functions: evacuation of fluid, opening of the lids, and application of drugs such as anesthetic or **antibiotics.** The present devices can include a sponge positioned around (a) an aspiration tube for withdrawing fluid and (b) an arm of a speculum. Other variations of the present devices include those with an aspiration tube for withdrawing fluid, the tube being positioned in a trough defined by an arm of a

speculum. Alternatively, the speculum arm can define a passage for holding the aspiration tube. In that alternate embodiment, the portion of the speculum arm defining the passage has openings for passing fluid into the passage so that the aspiration tube in the passage can then remove fluid.

Excerpt(s): This application is related to and claims priority benefits from U.S. Provisional Patent Application Serial No. 60/351,219 filed Jan. 22, 2002. The '219 provisional application is hereby incorporated by reference herein in its entirety. Aspects of the present invention are directed to the field of ophthalmic devices. More particularly, aspects of the present invention are directed to speculums for placement adjacent the sulcus, which is the region under the eyelid where the covering of the lid and globe fold back on themselves, during ophthalmic procedures. A class of instruments known as speculums facilitates access to the eye during ophthalmic procedures by spreading the lids. Speculums are of many designs but lid speculums work by using a wire or blade to wrap around the eyelid margin several millimeters near the midpoint to spread the eyelids gaining exposure of the ocular surfaces.

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

- **Pharmaceutically active aromatic guanylhydrazones**

  Inventor(s): Bacher, Gerald; (Germering, DE), Bevec, Dorian; (Germering, DE), Choidas, Axel; (Munich, DE), Hauber, Joachim; (Hamburg, DE), Keri, Gyorgy; (Budapest, HU), Obert, Sabine; (Munich, DE), Orfi, Laszlo; (Budapest, HU), Szekely, Istvan; (Budapest, HU)

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  Patent Application Number: 20030203969

  Date filed: January 7, 2003

  Abstract: The present invention relates to aromatic guanylhydrazone compounds and their use as pharmaceutically active agents, especially for prophylaxis and treatment of virally caused diseases and infections, including opportunistic infections. The inventive guanylhydrazone compounds are also useful as inhibitors of deoxyhypusine synthase and as inhibitors for nuclear export in infectious diseases and may be used to regulate bacterially induced TNF-.alpha. production. Furthermore, the aromatic guanylhydrazones exhibit antibacterial activity against Gram positive and Gram negative bacteria and can be regarded as a novel class of **antibiotics.** In addition, methods for prophylaxis and treatment of virally or bacterially induced infections and diseases are disclosed together with pharmaceutical compositions useful within said methods containing at least one aromatic guanylhydrazone of the present invention as active ingredient.

  Excerpt(s): The present invention relates to aromatic guanylhydrazone comunds and their use as pharmaceutically active agents, especially for prophylaxis and treatment of virally caused diseases and infections, including opportunistic infections. The inventive guanylhydrazone compounds are also useful as inhibitors of deoxyhypusine synthase and as inhibitors for nuclear export in infectious diseases and may be used to regulate the bacterially induced TNF-.alpha. production. Furthermore, the aromatic guanylhydrazones exhibit antibacterial activity against Gram positive and Gram negative bacteria and can be regarded as a novel class of **antibiotics.** In addition, methods for treating virally or bacterially induced infections and diseases are disclosed

together with pharmaceutical compositions useful within said methods. Deaths from what has since been recognized as HIV infection with immune failure have been seen clinically, without being understood, for at least 35 years, and probably much longer. An HIV-infected British sailor, who had traveled widely, is thought to have died with severe immune deficiency and HIV infection in 1959, the earliest proven case of modern AIDS. The genetic material of the most common HIV-1 strain is most similar to that of a virus known to naturally infect chimpanzees, and it may be that HIV's ancestors have been present in Africa, perhaps even in humans, for a very long time, perhaps thousands of years. In West Africa, a close cousin of the HIV-1, called HIV-2, is almost identical to several indigenous African monkey viruses, and almost certainly has been derived from them quite recently in virus evolutionary time (less than several centuries).

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

- **Preparation of quinoline-substituted carbonate and carbamate derivatives**

  Inventor(s): Allen, Michael S.; (Trevor, WI), Chang, Sou-Jen; (Prairie View, IL), Condon, Stephen; (Kenosha, WI), DeMattei, John A.; (Gurnee, IL), King, Steven A.; (Gurnee, IL), Kolaczkowski, Lawrence; (Gurnee, IL), Manna, Sukumar; (Libertyville, IL), Nichols, Paul J.; (Wildwood, IL), Patel, Hemant H.; (Ahmedabad, IN), Patel, Subhash R.; (Chicago, IL), Plata, Daniel J.; (Wadsworth, IL), Premchandran, Ramiya H.; (Gurnee, IL), Stoner, Eric J.; (Kenosha, WI), Tien, Jien-Heh J.; (Vernon Hills, IL), Wittenberger, Steven J.; (Mundelein, IL)

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  Patent Application Number: 20030199696

  Date filed: May 7, 2003

  Abstract: The invention relates to a process for preparing quinoline-substituted carbonate and carbamate compounds, which are important intermediates in the synthesis of 6-O-substituted macrolide **antibiotics.** The process employs metal-catalyzed coupling reactions to provide a carbonate or carbamate of formula (I) or (II) or a substrate that can be reduced to obtain the same.

  Excerpt(s): This application is a divisional of U.S. application Ser. No. 10/134,777 filed Apr. 29, 2002, which is a divisional application of U.S application Ser. No. 09/518,392 filed on Mar. 3, 2000, which claims priority from U.S. Provisional Application Serial No. 60/141,042, filed on Jun. 24, 1999. The present invention relates to the preparation of quinoline-substituted carbonate and carbamate derivatives, which provide important intermediates in the synthesis of 6-O-substituted macrolide **antibiotics.** In one aspect, the invention relates to the processes for preparing quinolyl-substituted carbonate or carbamate compounds and processes for preparing the compounds via an alkenol derivative. In another aspect, the invention relates to preparing carbonate or carbamate compounds via a quinoline carboxaldehyde or a derivative thereof. 6-O-Methylerythromycin A (clarithromycin) is a potent macrolide **antibiotic** disclosed in U.S. Pat. No. 4,331,803.

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

- **Quality rating tool for the health care industry**

  Inventor(s): Ho, Samuel W.; (Manhattan Beach, CA)

  Correspondence: JEFFER, MANGELS, BUTLER & MARMARO, LLP; 1900 AVENUE OF THE STARS, 7TH FLOOR; LOS ANGELES; CA; 90067; US

  Patent Application Number: 20030163349

  Date filed: February 28, 2002

  Abstract: A quality rating tool used for evaluating health care providers, such as medical groups or hospitals, and a method of creating a quality rating are described. A quality rating tool is organized based on medical groups and contains numerous measures that a health care consumer can use to determine a medical group best suited to the consumer's conditions and needs. The measures include safe dosing of pain killers, use of preferred **antibiotics,** and overuse of **antibiotics** in the clinical measures category and member cost pharmacy and member cost emergency room in the affordability measures category. Values in the quality rating for these measures and others are percentiles and, as such, inform the health care consumer of where a particular medical group ranked with respect to a specific measure. The quality rating tool is compiled by an organization having access to large volumes of consumer and physician data and data from numerous other sources such as hospitals and databases of pharmacy, emergency room, professional encounter claims data, as well as consumer complaint databases and survey forms.

  Excerpt(s): The present invention relates to methods of creating and providing a quality rating tool for evaluating service and treatment in the health care industry. In particular, it relates to methods relating to rating tools used to measure the quality of a treatment or service provided by a health care provider. Consumers, employers, business coalitions, government agencies and other organizations and individuals have long sought more detailed, meaningful information about health care providers. Presently, the health care industry provides information relating to quality of service at the health plan level. Quality information, also referred to as "report cards", at the level of health plans, fails to provide a health care consumer with sufficient information to make informed decisions regarding the consumer's health care needs. Information regarding the quality of service and treatment from a health care provider at a more granular level would allow a consumer to select from a group of health care providers better able to meet specific needs of the consumer. However, service and treatment quality information of health care providers at a more granular level would be of significant value to health care consumers as well as health care providers. Presently, when selecting a health care provider, such as a medical group, or when deciding on a physician, consumers are typically presented with a provider listing that states the geographic location of the provider and his or her specialty areas of practice, if applicable. In many cases, this is all the information consumers have to examine when making a decision on something as important as their health care provider.

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

- **Recombinant antibacterial group IIA phospholipase A2 and methods of use thereof**

  Inventor(s): Elsbach, Peter; (New York, NY), Liang, Ning-Sheng; (Nanning City, CN), Weiss, Jerrold; (Coralville, IA)

  Correspondence: DARBY & DARBY P.C.; Post Office Box 5257; New York; NY; 10150-5257; US

  Patent Application Number: 20030161822

  Date filed: September 25, 2002

  Abstract: Disclose herein is a novel recombinant mutant protein of human Group IIA phospholipase A2 (PLA2) which has enhanced antibacterial activity when compared to the wild-type human Group IIA PLA2, pharmaceutical formulations comprising the protein and methods of use thereof. Additionally, the formulations may comprise other bioactive compounds, such as, e.g., conventional **antibiotics,** that act additively or synergistically with Group IIA PLA2 in order to promote bacterial killing.

  Excerpt(s): This invention pertains to a novel recombinant mutant protein of human Group IIA Phospholipase A2 (PLA2) which has significantly enhanced antibacterial activity compared to the wild-type human Group IIA PLA2, pharmaceutical formulations comprising the protein and methods of use thereof. The growing prevalence of **antibiotic** resistance in bacterial pathogens has stimulated renewed interest in the discovery of novel **antibiotics.** U.S. Pat. No. 5,874,079 discloses that a "Group IIA" 14 kDa Phospholipase A2 (PLA2), mobilized during inflammation expresses potent bactericidal activity toward a broad range of clinically important Gram-positive bacteria and enhances the activity of the host defense mechanisms toward many Gram-negative bacteria. The phospholipase A2 (PLA2) family of enzymes hydrolyze the sn-2 ester of glycerophospholipids to produce a fatty acid and a lysophospholipid (Dennis, J. Biol. Chem. 269:13057-13060, 1994; Gelb et al, Ann. Rev. Biochem. 64, 653-688, 1995; Waite, The phospholipases, Plenum Press, New York, 1987). Based on amino acid sequences, 10 groups of PLA2s have been identified, including eight from mammals (Dennis, Trends Biochem. Sci. 22: 1-2, 1997; Cupillard et al., J. Biol. Chem. 272: 15745-15752, 1997). Group IIA PLA2 in mammals are produced by many different cell types including phagocytic cells, platelets, Paneth cells and lacrimal cells. It has been shown that both rabbit and human Group IIA PLA2 can, in concert with other host defense mechanisms, increase the destruction of gram-negative bacteria (Wright et al., J. Clin. Invest. 85: 1925-1935, 1990; Weiss et al., J. Biol. Chem. 269: 26331-26337, 1994 Elsbach et al., Trends Microbiol. 2: 324-328, 1994 and Madsen et al., Infect. Immun. 64: 2425-2430, 1996) and by itself, kill many gram-positive bacteria (Weinrauch et al., J. Clin. Invest. 97: 250-257, 1996). The antibacterial activity of Group IIA PLA2 appears to be a specific attribute of the mammalian 14 kDa isoform. This is further exemplified in experimentally induced local inflammatory (ascitic) fluid in rabbits, whereby the mobilization of Group IIA PLA2 is fully responsible for the potent bactericidal activity expressed in the fluid toward S. aureus and several other gram-positive bacteria (Weiss et al., en supra). Normal plasma, by contrast contains low levels of PLA2 and antistaphylococcal activity. It has recently been shown that the mobilization of this enzyme in baboons during inflammation may play an important role in host defense mechanisms against invading bacteria (Weinrauch et al., J. Clin. Invest. 102 (3): 633-638, 1998).

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

- **Regioselective and stereoselective oxidation of fused ring systems useful for the preparation of aminosterols**

  Inventor(s): Kinney, William A.; (Newtown, PA), Michalak, Ronald; (Congers, NY), Zhang, Xuehai; (US)

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  Patent Application Number: 20030171576

  Date filed: October 11, 2002

  Abstract: An efficient method for the synthesis of aminosterol compounds such as squalamine and compound 1436 is described. A method of the invention provides for regioselective oxidation and regioselective sulfonation of a fused ring system. The fused ring base can be, for example, a steroid ring base. The aminosterol compounds are effective as, for example, **antibiotics,** antiangiogenic agents and NHE3 inhibitors.

  Excerpt(s): The invention relates to a novel method of producing fused ring based compounds or aromatics including aminosterol compounds. A method of the invention offers regioselective oxidation and regioselective sulfonation of fused ring systems with few protecting groups. The aminosterol compounds produced by a method of the invention are useful as, among others, **antibiotics,** antiangiogenic agents and NHE3 inhibitors. Since the discovery of squalamine, however, several other interesting properties of this compound have been discovered. For example, as described in U.S. Pat. Nos. 5,733,899 and 5,721,226, squalamine may function as an antiangiogenic agent useful for the treatment of cancers. See U.S. Pat. No. 6,147,060. Additional uses of squalamine such as an agent for inhibiting NHE3 and as an agent for inhibiting endothelial cell growth are disclosed in U.S. Pat. No. 5,792,635. Methods for synthesizing squalamine have been described. See WO 94/19366 which relates to U.S. patent application. Ser. No. 08/023,347. U.S. Pat. No. 5,792,635 also discloses squalamine isolation and synthesis techniques.

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

- **Rice protein concentrate based organic nutritional formula**

  Inventor(s): Highman, Jay C.; (Westerville, OH), Liebrecht, Jeffrey Wayne; (Columbus, OH)

  Correspondence: Donald O. Nickey; 8765 Colvin Road; Plain City; OH; 43064; US

  Patent Application Number: 20030185941

  Date filed: March 27, 2002

  Abstract: This invention relates to a nutritional beverage substantially free of chemical pesticides, **antibiotics,** hormones, herbicides, non-genetically modified plants and chemical solvents that utilizes organic brown rice syrup and organic rice protein concentrate as major components and a source of calcium selected from various calcium salts, including mono-, di- or tricalcium phosphate, calcium lactate gluconate and mixtures thereof. The beverage preferably also contains water soluble vitamins, oil soluble vitamins and flavors. The use of rice protein concentrate stabilized with a blend of guar and CMC gums, and brown rice syrup provides a beverage with a smooth texture, a pleasant taste and a light, refreshing mouthfeel. The beverage also has excellent physical stability over shelf life.

Excerpt(s): This invention relates to an improved nutritional formula which is "organic" and possesses highly acceptable taste and mouth feel. The nutritional formula uses organic brown rice syrup as the major source of carbohydrates, non-solvent extracted edible oils as the source of lipids, and organic rice protein concentrate as the source of protein. A number of certification boards and some states, such as California, have procedures and regulations that must be followed for a food ingredient or food product to be labeled as "organic". One such board is the National Organic Standards Board (NOSB). The NOSB prohibits organic growers from using chemical pesticides, herbicides or fertilizers on their land for at least three years. NOSB standards currently allow up to 5 percent of the ingredients in nutritional products labeled "organic" to be non-organic, provided those ingredients are not widely available in organic form or on the USDA list of prohibited materials. The growing popularity of organic foods has reached a national level as well. For example, the United Stated Department of Agriculture's final national organic rule became effective on Apr. 21, 2001. There must be compliance with this law by Oct. 21, 2002. The consuming public is aware that organic foods reduce the health risks associated with consuming foods that are tainted with chemical solvents, pesticides, herbicides, and the like. While adults can carefully choose their source of nutrition, infants, toddlers and children are forced to consume liquid formulas that are not organic. One aspect of the present invention is directed to an infant formula and a nutritional beverage for toddlers and children that is greater than 95% organic. The invention is also directed to a "non-dairy" formulation based on organic rice protein concentrate as the sole source of protein. The invention is also directed to a method to prepare such nutritional beverages.

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

- **Specific and universal probes and amplification primers to rapidly detect and identify common bacterial pathogens and antibiotic resistance genes from clinical specimens for routine diagnosis in microbiology laboratories**

  Inventor(s): Bergeron, Michel G.; (Sillery, CA), Ouellette, Marc; (Quebec, CA), Roy, Paul H.; (Loretteville, CA)

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  Patent Application Number: 20030180733

  Date filed: April 11, 2002

  Abstract: The present invention relates to DNA-based methods for universal bacterial detection, for specific detection of the common bacterial pathogens Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, Streptococcus pneumoniae, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, Staphylococcus saprophyticus, Streptococcus pyogenes, Haemophilus influenzae and Moraxella catarrhalis as well as for specific detection of commonly encountered and clinically relevant bacterial **antibiotic** resistance genes directly from clinical specimens or, alternatively, from a bacterial colony. The above bacterial species can account for as much as 80% of bacterial pathogens isolated in routine microbiology laboratories.The core of this invention consists primarily of the DNA sequences from all species-specific genomic DNA fragments selected by hybridization from genomic libraries or, alternatively, selected from data banks as well as any oligonucleotide sequences derived from these sequences which can be used as probes or amplification primers for PCR or any other nucleic acid amplification methods. This invention also includes DNA

sequences from the selected clinically relevant **antibiotic** resistance genes.With these methods, bacteria can be detected (universal primers and/or probes) and identified (species-specific primers and/or probes) directly from the clinical specimens or from an isolated bacterial colony. Bacteria are further evaluated for their putative susceptibility to **antibiotics** by resistance gene detection (antibiotic resistance gene specific primers and/or probes). Diagnostic kits for the detection of the presence, for the bacterial identification of the above-mentioned bacterial species and for the detection of **antibiotic** resistance genes are also claimed. These kits for the rapid (one hour or less) and accurate diagnosis of bacterial infections and **antibiotic** resistance will gradually replace conventional methods currently used in clinical microbiology laboratories for routine diagnosis. They should provide tools to clinicians to help prescribe promptly optimal treatments when necessary. Consequently, these tests should contribute to saving human lives, rationalizing treatment, reducing the development of **antibiotic** resistance and avoid unnecessary hospitalizations.

Excerpt(s): Bacteria are classically identified by their ability to utilize different substrates as a source of carbon and nitrogen through the use of biochemical tests such as the API20E.TM. system. Susceptibility testing of Gram negative bacilli has progressed to microdilution tests. Although the API and the microdilution systems are cost-effective, at least two days are required to obtain preliminary results due to the necessity of two successive overnight incubations to isolate and identify the bacteria from the specimen. Some faster detection methods with sophisticated and expensive apparatus have been developed. For example, the fastest identification system, the autoSCAN-Walk-Away system.TM. identifies both Gram negative and Gram positive from isolated bacterial colonies in 2 hours and susceptibility patterns to **antibiotics** in only 7 hours. However, this system has an unacceptable margin of error, especially with bacterial species other than Enterobacteriaceae (York et al., 1992. J. Clin. Microbiol. 30:2903-2910). Nevertheless, even this fastest method requires primary isolation of the bacteria as a pure culture, a process which takes at least 18 hours if there is a pure culture or 2 to 3 days if there is a mixed culture. A large proportion (40-50%) of specimens received in routine diagnostic microbiology laboratories for bacterial identification are urine specimens (Pezzlo, 1988, Clin. Microbiol. Rev. 1:268-280). Urinary tract infections (UTI) are extremely common and affect up to 20% of women and account for extensive morbidity and increased mortality among hospitalized patients (Johnson and Stamm, 1989; Ann. Intern. Med. 111:906-917). UTI are usually of bacterial etiology and require antimicrobial therapy. The Gram negative bacillus Escherichia coli is by far the most prevalent urinary pathogen and accounts for 50 to 60% of UTI (Pezzlo, 1988, op. cit.). The prevalence for bacterial pathogens isolated from urine specimens observed recently at the "Centre Hospitalier de 1'Universit Laval (CHUL)" is given in Tables 1 and 2. Conventional pathogen identification in urine specimens. The search for pathogens in urine specimens is so preponderant in the routine microbiology laboratory that a myriad of tests have been developed. The gold standard is still the classical semi-quantitative plate culture method in which a calibrated loop of urine is streaked on plates and incubated for 18-24 hours. Colonies are then counted to determine the total number of colony forming units (CFU) per liter of urine. A bacterial UTI is normally associated with a bacterial count of.gtoreq.10.sup.7 CFU/L in urine. However, infections with less than 10.sup.7 CFU/L in urine are possible, particularly in patients with a high incidence of diseases or those catheterized (Stark and Maki, 1984, N. Engl. J. Med. 311:560-564). Importantly, close to 80% of urine specimens tested are considered negative (<10.sup.7 CFU/L; Table 3).

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

- **Stabilized nucleic acids in gene and drug discovery and methods of use**

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  Patent Application Number: 20030170694

  Date filed: December 20, 2002

  Abstract: Stabilized nucleic acids for use in gene and drug discovery are disclosed. Vectors and host cells useful in the production of stabilized nucleic acids are also disclosed. Cell-based assays which employ stabilized antisense nucleic acids to identify and develop **antibiotics** and to identify genes required for proliferation are described. The use of stabilized nucleic acids to identify homologous nucleic acids required for the proliferation of heterologous organisms is also described. Inhibition of the expression of genes required for proliferation in heterologous organisms through the use of stabilized antisense nucleic acids is disclosed.

  Excerpt(s): This application claims priority to U.S. Provisional Patent Application Serial No. 60/343,512, filed Dec. 21, 2001, by Daniel Wall, et al., and entitled "STABILIZED NUCLEIC ACIDS IN GENE AND DRUG DISCOVERY AND METHODS OF USE", the disclosure of which is incorporated herein by reference in its entirety. Since the discovery of penicillin, the use of **antibiotics** to treat the ravages of bacterial infections has saved millions of lives. With the advent of these "miracle drugs," for a time it was popularly believed that humanity might, once and for all, be saved from the scourge of bacterial infections. In fact, during the 1980s and early 1990s, many large pharmaceutical companies cut back or eliminated **antibiotics** research and development. They believed that infectious disease caused by bacteria finally had been conquered and that markets for new drugs were limited. Unfortunately, this belief was overly optimistic. The tide is beginning to turn in favor of the bacteria as reports of drug resistant bacteria become more frequent. The United States Centers for Disease Control announced that one of the most powerful known **antibiotics,** vancomycin, was unable to treat an infection of the common Staphylococcus aureus (staph). This organism is commonly found in our environment and is responsible for many nosocomial infections. The import of this announcement becomes clear when one considers that vancomycin was used for years to treat infections caused by Staphylococcus species as well as other stubborn strains of bacteria. In short, bacteria are becoming resistant to our most powerful **antibiotics.** If this trend continues, it is conceivable that we will return to a time when what are presently considered minor bacterial infections are fatal diseases.

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

- **Sublancin lantibiotic produced by Bacillus subtilis 168**

  Inventor(s): Hansen, J. Norman; (Silver Spring, MD)

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  Patent Application Number: 20030166835

  Date filed: February 25, 2003

  Abstract: An antimicrobial peptide produced by Bacillus subtilis 168 was isolated and characterized and named sublancin 168. The invention includes DNA encoding for the

sublancin 168 peptides and peptides which are at least 80% identical to the sublancin 168 peptide. The peptides may be administered as anti-bacterials, or may be used in food preservation. The peptides may also be co-administered with other lantibiotics (such as nisin and subtilin), or with known **antibiotics.**

Excerpt(s): The invention relates to novel bacterially-produced antimicrobial peptides; more particularly the invention relates to a dehydroalanine-containing lantibiotic. Lantibiotics are bacterially-produced antimicrobial peptides that possess unique chemical and biological properties owing to their containing a variety of unusual amino acid residues. Lantibiotics are defined as such by the presence of lanthionine or.beta.-methyllanthionin- e, which are introduced by a posttranslational process in which serine or threonine is dehydrated to the corresponding dehydro residue, which then reacts in a Michael-type addition of a cysteine sulfhydryl group to the double bond of the dehydro residue to form a thioether link [reviewed in (1-6)]. Mature lantibiotics typically contain one or more dehydro residues that do not participate in lanthionine bridges. The unique properties that are conferred by these unusual residues results in their being useful components in the design of novel biomolecules (1,2,7,8). One of the attractive features of lantibiotics is that they are comprised of gene-encoded polypeptide sequences, so their structures can be manipulated by protein engineering. Whereas this is simple in concept, putting it into practice requires the utilization of many different genetic and recombinant DNA techniques, including the removal and replacement of chromosomal segments with their genetically-engineered counterparts. Ideally, these manipulations need to be done in such a way that the engineered lantibiotic analog be efficiently produced so that useful amounts of the analog are available for experimentation, which implies a need to engineer regulatory elements. Only a few bacterial strains have been sufficiently characterized to permit these manipulations to be performed in a convenient and facile manner. One such well-characterized bacterial strain is Bacillus subtilis 168, which is second only to E. coli in the extent to which tools of genetic and protein engineering have been developed, which has contributed to the extensive use of B. subtilis 168 for the industrial production of bio-engineered materials. The advantage of B. subtilis 168 over other bacterial strains has recently been increased even more by the availability of the complete sequence of the B. subtilis 168 genome (9).

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

- **Therapeutic and protective dental device useful as an intra-oral delivery system**

  Inventor(s): Bardach, Laura; (Boonton, NJ), Geduldig, James; (Boonton, NJ), Napoli, Salvatore; (Maywood, NJ)

  Correspondence: LERNER, DAVID, LITTENBERG,; KRUMHOLZ & MENTLIK; 600 SOUTH AVENUE WEST; WESTFIELD; NJ; 07090; US

  Patent Application Number: 20030205234

  Date filed: May 6, 2002

  Abstract: A dental device has a U-shaped carrier with at least one channel for embracing an arch of teeth. The carrier has recessed insets in the channel. Discrete inserts carrying a beneficial agent can fit into the insets and release the agent gradually. When the device is used in a primarily therapeutic application, the inserts may be installed into all or less than all of the insets to form various insert patterns. Thus, different oral regions can be affected by different insert patterns. When the device is used as an athletic mouthguard, temporary blanks may be initially fitted in the insets, while a portion of the mouthguard is softened before an arch of teeth is pressed into the channel to make a custom

impression. The inserts that are later installed in the insets possess different physical properties than the carrier and may be positioned and shaped to mechanically buffer teeth of the arch from mechanical shocks as well as release beneficial agents. The inserts may be replaced or refreshed to maintain the beneficial agent, which may be xylitol, remineralizing agents, moisturizing agents, desensitizing agents, flavoring agents, breath fresheners, chemical and biological indicators, nutraceuticals, **antibiotics,** probiotics, other medications and chemotherapeutics, or other agents.

Excerpt(s): The present invention relates to dental devices that are worn on an arch of teeth, and in particular, to devices that can deliver a beneficial agent to, and protect the teeth and soft tissues from mechanical, chemical and biologic injury. Mouthguards are typically made from plastics materials such as an ethylene vinyl acetate copolymer (EVA). Other devices such as dentoalveolar trays, carriers and splints may be made of EVA or other biocompatible plastic material. There are several categories of mouthguards: Mouthguards that are stock pre-molded products and made in a variety of sizes, home or self-moldable to suit the physical characteristics of the user, or custom molded by a dentist or other professional to suit the characteristics of the user. Regarding physical protection, stock mouthguards are typically the cheapest and least effective in use while the custom molded and shaped mouthguards are the most expensive and effective in their impact absorbent properties. Athletes in many sports wear mouthguards for prolonged periods. It is common knowledge that when these athletes engage in strenuous physical activity, they lose and must replace significant amounts of fluids, nutrients and calories. In order to hydrate themselves, and replenish their energy, athletes must drink large quantities of fluids and eat foods that are very often cariogenic. These cariogenic fluids and materials cover the teeth, and when a mouthguard is inserted afterwards, the teeth are acted upon by cariogenic bacteria in an ideal environment, shielded from the buffering ability of saliva.

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

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You can also use this procedure to view pending patent applications concerning antibiotics. 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 ANTIBIOTICS

## Overview

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

- **Antibiotic and Antimicrobial Use in Dental Practice**

  Source: Chicago, IL: Quintessence Publishing Co, Inc. 2001. 288 p.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $32.00 plus shipping and handling. ISBN: 0867153970.

  Summary: Antibiotics and antimicrobials have become an integral and critical part of dental practice. This textbook integrates basic facts and principles of antibiotic therapy with recently-emerged concepts of care. The text includes 19 chapters in five sections: general principles, drugs of choice, adverse reactions, clinical applications, and special considerations. Topics include principles of antimicrobial chemotherapy in dental and orofacial infections, microbiological sampling and sensitivity testing, individual drugs, general principles and individual topical antimicrobial agents, topical and systemic

antifungal and antiviral agents, allergic and other sensitivity reactions, adverse microbiological effects, antibiotics in periodontal therapy, oral malodor (halitosis, or bad breath), antibiotics in endodontic (root canal) therapy, antibiotics for oral and maxillofacial infections, pediatric considerations, chemotherapeutic agents in restorative dentistry, antimicrobials in implant dentistry, prophylactic antibiotic use, antimicrobial therapy for immunocompromised patients, considerations for female patients, patients with common systemic diseases, and legal considerations. In each chapter, important principles, key facts, and clinical insights are highlighted; chapters conclude with a list of references. The book concludes with appendices and a subject index; a quick reference guide is also offered that guides readers to summaries of information about general principles, drug selection, pharmacokinetics, drug interactions and adverse effects, and prophylaxis and prevention. The text is illustrated with charts, figures, and a few black and white photographs.

- **Beyond Antibiotics: 50 (Or So) Ways to Boost Immunity and Avoid Antibiotics**

  Contact: North Atlantic Books, PO Box 12327, Berkeley, CA, 94701-9998, (510) 559-8277.

  Summary: This monograph examines the reported overuse of antibiotics in medicine and the problems caused by the creation of antibiotic-resistant bacteria. The authors, physicians who describe themselves as holistic doctors, propose minimizing the use of antibiotics through enhancing health, boosting resistance to illness, and using preventive strategies. They analyze evidence indicating that diet, nutrition, lifestyle, environment, and stress have an important impact on resistance to infection. A section on natural medicine explores the use of vitamins, herbal medicine, homeopathy, and other natural methods for strengthening immunity. The final section offers "selfcare" and "wellcare" alternatives for treating conditions for which antibiotics are usually prescribed, such as fever, vaginitis, sinusitis, and intestinal infections with diarrhea.

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

- **Advanced Technologies in Research, Diagnosis and Treatment of AIDS and in Oncology: International Workshop, Naples, October 21-22, 1993 (Antibiotics)** by G. Giraldo, et al (1994); ISBN: 3805559704; http://www.amazon.com/exec/obidos/ASIN/3805559704/icongroupinterna
- **Analysis of Antibiotic/Drug Residues in Food Products of Animal Origin** by Vipin K. Agarwal (Editor) (1992); ISBN: 0306441993; http://www.amazon.com/exec/obidos/ASIN/0306441993/icongroupinterna
- **Antibiotic and Antimicrobial Use in Dental Practice** by Michael G. Newman (Editor), et al (2001); ISBN: 0867153970; http://www.amazon.com/exec/obidos/ASIN/0867153970/icongroupinterna

- **Antibiotic and Chemotherapy** by Harold P. Lambert, Francis W. O'Grady (Editor) (1992); ISBN: 0443032033; http://www.amazon.com/exec/obidos/ASIN/0443032033/icongroupinterna
- **Antibiotic and Chemotherapy: Anti-Infective Agents and Their Use in Therapy** by Roger Finch (Editor), et al (2003); ISBN: 0443071292; http://www.amazon.com/exec/obidos/ASIN/0443071292/icongroupinterna
- **Antibiotic and Chemotherapy: Anti-Infective Agents and Their Use in Therapy** by Francis O'Grady, Lambert (2003); ISBN: 0443052557; http://www.amazon.com/exec/obidos/ASIN/0443052557/icongroupinterna
- **Antibiotic Crisis, Antibiotic Alternatives** by Leon Chaitow (1998); ISBN: 0722537727; http://www.amazon.com/exec/obidos/ASIN/0722537727/icongroupinterna
- **Antibiotic Essentials, 2003** by Burke A. Cunha (2003); ISBN: 1890114413; http://www.amazon.com/exec/obidos/ASIN/1890114413/icongroupinterna
- **Antibiotic Resistance** by Carlos Amabile-Cuevas (2003); ISBN: 1587061082; http://www.amazon.com/exec/obidos/ASIN/1587061082/icongroupinterna
- **Antibiotic Resistance : Origins, Evolution, Selection and Spread - Symposium No. 207** by CIBA Foundation Symposium (Author) (1997); ISBN: 0471971057; http://www.amazon.com/exec/obidos/ASIN/0471971057/icongroupinterna
- **Antibiotic Resistance Genes: Ecology, Transfer, and Expression (Banbury Report, 24)** by Stuart B. Levy, Richard P. Novick (Editor) (1987); ISBN: 0879692243; http://www.amazon.com/exec/obidos/ASIN/0879692243/icongroupinterna
- **Antibiotic Resistance Transfer in the Mammalian Intestinal Tract** by Abigail A. Salyers (1995); ISBN: 1570592977; http://www.amazon.com/exec/obidos/ASIN/1570592977/icongroupinterna
- **Antibiotic Resistance: a Concern for All (NT Clinical Monographs)** by David Taylor (1999); ISBN: 1902499603; http://www.amazon.com/exec/obidos/ASIN/1902499603/icongroupinterna
- **Antibiotic Selection in Obstetrics and Gynecology** by Gilles R. G. Monif (1996); ISBN: 1880906076; http://www.amazon.com/exec/obidos/ASIN/1880906076/icongroupinterna
- **Antibiotic Therapy in Head and Neck Surgery (Science and Practice of Surgery, No 11)** by Jonas T. Johnson (Editor) (1987); ISBN: 0824776712; http://www.amazon.com/exec/obidos/ASIN/0824776712/icongroupinterna
- **Antibiotic-Resistant Microbes: Global Superbugs; Global Killers [DOWNLOAD: ADOBE READER]** by Richard C. Honour (2003); ISBN: B0000E2Y3H; http://www.amazon.com/exec/obidos/ASIN/B0000E2Y3H/icongroupinterna
- **Antibiotics & Other Secondary Metabolites: Biosynthesis & Production** by Hatter, R. V. P. Hutter (Editor) (1997); ISBN: 0123632501; http://www.amazon.com/exec/obidos/ASIN/0123632501/icongroupinterna
- **Antibiotics (Great Medical Discoveries)** by Evelyn B. Kelly , Lucent Books (2005); ISBN: 1560069252; http://www.amazon.com/exec/obidos/ASIN/1560069252/icongroupinterna
- **Antibiotics and Adverse Effects: Medical Subject Analysis and Research Guidebook With Bibliography** by Katie Lee Holt (1987); ISBN: 0881642908; http://www.amazon.com/exec/obidos/ASIN/0881642908/icongroupinterna

- **Antibiotics and Antiviral Compounds** (1993); ISBN: 1560817453; http://www.amazon.com/exec/obidos/ASIN/1560817453/icongroupinterna
- **Antibiotics and Microbial Transformations** by Surendar S. Lamba, Charles A. Walker (Editor) (1987); ISBN: 0849364086; http://www.amazon.com/exec/obidos/ASIN/0849364086/icongroupinterna
- **Antibiotics for Animals: The Antibiotic Resistance Issue (Comments from Cast, 1989-2)** by Virgil W. Hays (1989); ISBN: 9999222935; http://www.amazon.com/exec/obidos/ASIN/9999222935/icongroupinterna
- **Antibiotics I: B-Lactams and Other Antimicrobial Agents (Japanese Technology Reviews)** by Isao Kawamoto (1992); ISBN: 2881248551; http://www.amazon.com/exec/obidos/ASIN/2881248551/icongroupinterna
- **Antibiotics II: Antiobiotics by Fermentation (Japanese Technology Reviews)** by Sadao Teshiba (1993); ISBN: 2881248896; http://www.amazon.com/exec/obidos/ASIN/2881248896/icongroupinterna
- **Antibiotics in the Tropics** (1988); ISBN: 3540186832; http://www.amazon.com/exec/obidos/ASIN/3540186832/icongroupinterna
- **Antibiotics in the Tropics: Antibacterial Therapy With Limited Resources** by S. Enenkel, W. Stille (1988); ISBN: 0387186832; http://www.amazon.com/exec/obidos/ASIN/0387186832/icongroupinterna
- **Antibiotics Pocketcard (Package of 10 Cards with Display)** by Borm Bruckmeier Publishing (2002); ISBN: 1591030048; http://www.amazon.com/exec/obidos/ASIN/1591030048/icongroupinterna
- **Antibiotics Pocketcard 2003 (10 Copy Display Package)** by Borm Bruckmeier Publishers (2003); ISBN: 1591031125; http://www.amazon.com/exec/obidos/ASIN/1591031125/icongroupinterna
- **Antibiotics, Antibacterial Agents and Antifungals** by Andre Bryskier (Editor) (2004); ISBN: 1555812376; http://www.amazon.com/exec/obidos/ASIN/1555812376/icongroupinterna
- **Antibiotics: A Multidisciplinary Approach** by Giancarlo Lancini, et al (1995); ISBN: 0306449242; http://www.amazon.com/exec/obidos/ASIN/0306449242/icongroupinterna
- **Antibiotics: Actions, Origins, Resistance** by Christopher Walsh (2003); ISBN: 1555812546; http://www.amazon.com/exec/obidos/ASIN/1555812546/icongroupinterna
- **Bacterial Meningitis (Antibiotics and Chemotherapy, Vol 45)** by H. Schonfeld, et al (1992); ISBN: 3805554842; http://www.amazon.com/exec/obidos/ASIN/3805554842/icongroupinterna
- **Bacteriophage As Antibiotics: Molecular Biology and Applications** by Elizabeth Kutter, Alexander Sulakvelidze (2004); ISBN: 0849313368; http://www.amazon.com/exec/obidos/ASIN/0849313368/icongroupinterna
- **Battling Resistance to Antibiotics and Pesticides: An Economic Approach** by Ramanan Laxminarayan (Editor) (2003); ISBN: 1891853511; http://www.amazon.com/exec/obidos/ASIN/1891853511/icongroupinterna

- **Beta-Lactum Antibiotics for Clinical Use (Clinical Pharmacology Series, Vol 4)** by Sherry F. Queener (Editor) (1986); ISBN: 0824773861; http://www.amazon.com/exec/obidos/ASIN/0824773861/icongroupinterna
- **Beyond Antibiotics: 50 (Or So) Ways to Boost Immunity and Avoid Antibiotics** by Michael A. Schmidt, et al (1994); ISBN: 1556431805; http://www.amazon.com/exec/obidos/ASIN/1556431805/icongroupinterna
- **Biochemistry of Peptide Antibiotics** by Horst Kleinkauf (Editor), Hans Von Dohren (Editor) (1990); ISBN: 3110119285; http://www.amazon.com/exec/obidos/ASIN/3110119285/icongroupinterna
- **Biomedical and Social Developments in AIDS and Associated Tumors (Antibiotics and Chemotherapy, Vol 43)** by Advanced Course on Aides and Associated Tumors, G. Giraldo (1991); ISBN: 380555303X; http://www.amazon.com/exec/obidos/ASIN/380555303X/icongroupinterna
- **Biotechnology of Antibiotics and Other Bioactive Microbial Metabolites** by Giancarlo Lancini, Rolando Lorenzetti (1994); ISBN: 0306446030; http://www.amazon.com/exec/obidos/ASIN/0306446030/icongroupinterna
- **Cancer Management in Man: Biological Response Modifiers, Chemotherapy, Antibiotics, Hyperthermia, Supporting Measures (Cancer Growth and Progression)** by Paul V. Woolley (Editor) (1989); ISBN: 0898389992; http://www.amazon.com/exec/obidos/ASIN/0898389992/icongroupinterna
- **Chemical Analysis for Antibiotics Used in Agriculture** by Hisao Oka (Editor) (1995); ISBN: 0935584579; http://www.amazon.com/exec/obidos/ASIN/0935584579/icongroupinterna
- **Clinical Pharmacokinetics of Sulfonamides and Their Metabolites (Antibiotics and Chemotherapy, Vol 37)** by Tom B. Vree (Editor) (1987); ISBN: 3805545118; http://www.amazon.com/exec/obidos/ASIN/3805545118/icongroupinterna
- **Clinician's Manual on Antibiotic Prescribing in the Community** by Erwin Brown (2000); ISBN: 1858739160; http://www.amazon.com/exec/obidos/ASIN/1858739160/icongroupinterna
- **Colloidal Silver : Antibiotic Superhero** by Johnny Silverseed (2001); ISBN: 0970825609; http://www.amazon.com/exec/obidos/ASIN/0970825609/icongroupinterna
- **CRC Handbook of Antibiotic Compounds** (1987); ISBN: 0849334342; http://www.amazon.com/exec/obidos/ASIN/0849334342/icongroupinterna
- **Development and Applications of Vaccines and Gene Therapy in AIDS (Antibiotics and Chemotherapy, Vol. 48)** by G. Giraldo (Editor) (1996); ISBN: 380556256X; http://www.amazon.com/exec/obidos/ASIN/380556256X/icongroupinterna
- **Do-It-Yourself Medicine : How To Find And Use The Most Effective Antibiotics, Painkillers, Anesthetics And Other Miracle Drugs. Without Costly Doctors' Prescriptions Or Hospitals** by Ragnar Benson (Author) (1997); ISBN: 0873649184; http://www.amazon.com/exec/obidos/ASIN/0873649184/icongroupinterna
- **Fluoroquinolone Antibiotics** by Don E. Low (Editor), et al (2003); ISBN: 3764365919; http://www.amazon.com/exec/obidos/ASIN/3764365919/icongroupinterna
- **Frontiers in Microbiology: From Antibiotics to AIDS (New Perspectives in Clinical Microbiology)** by Erik De Clercq (Editor) (1987); ISBN: 0898389593; http://www.amazon.com/exec/obidos/ASIN/0898389593/icongroupinterna

- **Genetics and Biochemistry of Antibiotic Production (Biotechnology, No 28)** by Colin Stuttard (Editor), Leo Vining (Editor) (1995); ISBN: 075069095X; http://www.amazon.com/exec/obidos/ASIN/075069095X/icongroupinterna
- **Government Response to the House of Lords Select Committee on Science and Technology Report: Resistance to Antibiotics and Other Antimicrobial Agents (Cm: 4172)** (1998); ISBN: 0101417225; http://www.amazon.com/exec/obidos/ASIN/0101417225/icongroupinterna
- **Guideline for the Format and Content: The Summary for New Drug and Antibiotic Applications** by BPI Information Services (1987); ISBN: 1579791611; http://www.amazon.com/exec/obidos/ASIN/1579791611/icongroupinterna
- **Guideline on Formatting, Assembling, and Submitting New Drug and Antibiotic Applications** by BPI Information Services (1987); ISBN: 1579791603; http://www.amazon.com/exec/obidos/ASIN/1579791603/icongroupinterna
- **Handbook of Essential Antibiotics** by Geoffrey M. Scoff (Editor), S. Ky May (Editor) (2004); ISBN: 9058231755; http://www.amazon.com/exec/obidos/ASIN/9058231755/icongroupinterna
- **Herbal Antibiotics: Natural Alternatives for Treating Drug-Resistant Bacteria (Storey Medicinal Herb Guide)** by Stephen Harrod Buhner, Stephen Harrod Buhne (1999); ISBN: 1580171486; http://www.amazon.com/exec/obidos/ASIN/1580171486/icongroupinterna
- **Icss 254, Antibiotic Resistance in Cystic Fibrosis -An Emerging Crisis?** by Tyrone Pitt (2003); ISBN: 185315539X; http://www.amazon.com/exec/obidos/ASIN/185315539X/icongroupinterna
- **Influence of Antibiotics on the Host-Parasite Relationship III** (1989); ISBN: 3540192239; http://www.amazon.com/exec/obidos/ASIN/3540192239/icongroupinterna
- **King Guide to Antibiotic and Chemotherapy Admixtures** by James C. King, Patrick N. Catania (2001); ISBN: 0970190255; http://www.amazon.com/exec/obidos/ASIN/0970190255/icongroupinterna
- **Kirk-Othmer Encyclopedia of Chemical Technology, Alkanolamines to Antibiotics (Glycopeptides)** by Jacqueline I. Kroschwitz, et al (1992); ISBN: 0471526703; http://www.amazon.com/exec/obidos/ASIN/0471526703/icongroupinterna
- **Kirk-Othmer Encyclopedia of Chemical Technology, Antibiotics (β-Lactams) to Batteries** by Jacqueline I. Kroschwitz (Editor), et al (1992); ISBN: 0471526711; http://www.amazon.com/exec/obidos/ASIN/0471526711/icongroupinterna
- **Lantibiotics and Related Peptides (Biotechnology Intelligence Unit)** by Ralph W. Jack, et al (1998); ISBN: 3540636005; http://www.amazon.com/exec/obidos/ASIN/3540636005/icongroupinterna
- **Launching the Antibiotic Era** by Carol Moberg (Editor), Zanvil A. Cohn (1990); ISBN: 0874700477; http://www.amazon.com/exec/obidos/ASIN/0874700477/icongroupinterna
- **Macrolide Antibiotics: Chemistry, Biology, and Practice, Second Edition** by Satoshi Omura (Editor) (2002); ISBN: 0125264518; http://www.amazon.com/exec/obidos/ASIN/0125264518/icongroupinterna

- **Magic Bullets, Lost Horizons: The Rise and Fall of Antibiotics** by Sebastian Amyes, Sebatian G. B. Amyes (2003); ISBN: 0415272033; http://www.amazon.com/exec/obidos/ASIN/0415272033/icongroupinterna
- **Miracle Cure: The Story of Penicillin and the Golden Age of Antibiotics** by Milton Wainwright, John Wainwright (1990); ISBN: 0631164928; http://www.amazon.com/exec/obidos/ASIN/0631164928/icongroupinterna
- **Natural Alternatives to Antibiotics** by John McKenna (1998); ISBN: 0895298392; http://www.amazon.com/exec/obidos/ASIN/0895298392/icongroupinterna
- **Nature's Antibiotics** by Kate Gilbert Udall (1997); ISBN: 1885670931; http://www.amazon.com/exec/obidos/ASIN/1885670931/icongroupinterna
- **No More Amoxicillin: Preventing and Treating Ear and Respiratory Infections Without Antibiotics** by Mary Ann Block (1998); ISBN: 1575663163; http://www.amazon.com/exec/obidos/ASIN/1575663163/icongroupinterna
- **Not All Bugs Need Drugs: A Guide for Parents to the Safe Use of Antibiotics** (2002); ISBN: 1902030702; http://www.amazon.com/exec/obidos/ASIN/1902030702/icongroupinterna
- **Oral Cephalosporins (Antibiotics and Chemotherapy, Vol 47)** by R. C., Jr Moellering (Editor) (1995); ISBN: 3805561636; http://www.amazon.com/exec/obidos/ASIN/3805561636/icongroupinterna
- **Origin, Evolution and Spread of Antibiotic Resistance Genes (Molecular Biology Intelligence Unit)** by Carlos F. Amabile-Cuevas (1993); ISBN: 1570592748; http://www.amazon.com/exec/obidos/ASIN/1570592748/icongroupinterna
- **Overkill: How Our Nation's Abuse of Antibiotics and Other Germ Killers Is Hurting Your Health and What You Can Do About It** by Kimberly Thompson, et al (2002); ISBN: 1579545343; http://www.amazon.com/exec/obidos/ASIN/1579545343/icongroupinterna
- **Peptide Antibiotics: Discovery, Modes of Action, and Applications** by Christopher J. Dutton (Editor), et al (2002); ISBN: 082470245X; http://www.amazon.com/exec/obidos/ASIN/082470245X/icongroupinterna
- **Pharmacokinetics of Selected Antibacterial Agents (Antibiotics and Chemotherapy, Vol. 49)** by Axel Dalhoff (1998); ISBN: 3805565763; http://www.amazon.com/exec/obidos/ASIN/3805565763/icongroupinterna
- **Pharmacoknetics of Sulfonamides Revisited (Antibiotics and Chemotherapy, Vol 34)** by Tom B. Vree (1986); ISBN: 3805539495; http://www.amazon.com/exec/obidos/ASIN/3805539495/icongroupinterna
- **Post Penicillin Antibiotics: from Acceptance to Resistance (Wellcome Witnesses to Twentieth Century Medicine)** by E.M. Tansey (Editor), L.A. Reynolds (Editor) (2000); ISBN: 1841290122; http://www.amazon.com/exec/obidos/ASIN/1841290122/icongroupinterna
- **Process Development in Antibiotic Fermentations** by C. T. Calam (Author) (2003); ISBN: 0521304903; http://www.amazon.com/exec/obidos/ASIN/0521304903/icongroupinterna
- **Recent Advances in AIDS and Kaposi's Sarcoma (Antibiotics and Chemotherapy, Vol 38)** by E. Giraldo, et al (1987); ISBN: 3805545126; http://www.amazon.com/exec/obidos/ASIN/3805545126/icongroupinterna

- **Recent Progress in the Chemical Synthesis of Antibiotics and Related Microbial Products** (1993); ISBN: 3540567542; http://www.amazon.com/exec/obidos/ASIN/3540567542/icongroupinterna
- **Regional Chemotherapy (Antibiotics and Chemotherapy, Vol 40)** by U. Laffer, et al (1988); ISBN: 380554670X; http://www.amazon.com/exec/obidos/ASIN/380554670X/icongroupinterna
- **Report on Microbial Antibiotic Resistance in Relation to Food Safety** (1999); ISBN: 0113222831; http://www.amazon.com/exec/obidos/ASIN/0113222831/icongroupinterna
- **Resistance to Antibiotics and Other Antimicrobial Agents (HL Paper)** (1998); ISBN: 0104788984; http://www.amazon.com/exec/obidos/ASIN/0104788984/icongroupinterna
- **Resolving the Antibiotic Paradox: Progress in Understanding Drug Resistance and Developments of New Antibiotics (Advances in Experimental Medicine and Biology, 456)** by Barry P. Rosen (Editor), Shahriar Mobashery (Editor) (1998); ISBN: 0306460394; http://www.amazon.com/exec/obidos/ASIN/0306460394/icongroupinterna
- **Select Committee on Science and Technology 7th Report: Resistance to Antibiotics House of Lords Paper 81-I Session, 1997-98** by Great Britain (1998); ISBN: 0104789980; http://www.amazon.com/exec/obidos/ASIN/0104789980/icongroupinterna
- **Strategies for Antibiotic Usage and Utilization Review** by Timothy R. Franson (1987); ISBN: 0960333282; http://www.amazon.com/exec/obidos/ASIN/0960333282/icongroupinterna
- **Supportive Care in Cancer Patients: Recent Developments (Antibiotics and Chemotherapy,Vol 50)** by Meinolf Karthaus (Editor), Arnold Ganser (Editor) (1999); ISBN: 3805569106; http://www.amazon.com/exec/obidos/ASIN/3805569106/icongroupinterna
- **Synthetic Aspects of Aminodeoxy Sugars of Antibiotics** by I.F. Pelyvas, et al (1988); ISBN: 0387188770; http://www.amazon.com/exec/obidos/ASIN/0387188770/icongroupinterna
- **The Antibiotic Paradox: How the Misuse of Antibiotics Destroys Their Curative Powers** by Stuart B., MD Levy, M.D., Stuart B. Levy (2002); ISBN: 0738204404; http://www.amazon.com/exec/obidos/ASIN/0738204404/icongroupinterna
- **The Biological Cost of Resistance to Antibiotics (Comprehensive Summaries of Uppsala Dissertations from the Faculty of sciencE and Technology, 539)** by Johanna Bjorkman (2000); ISBN: 9155447201; http://www.amazon.com/exec/obidos/ASIN/9155447201/icongroupinterna
- **The Chemistry of Antitumor Antibiotics** by William Alan Remers (1988); ISBN: 0471081809; http://www.amazon.com/exec/obidos/ASIN/0471081809/icongroupinterna
- **The Enterococci: Pathogenesis, Molecular Biology, and Antibiotic Resistance** by Michael S. Gilmore (Editor), et al (2002); ISBN: 1555812341; http://www.amazon.com/exec/obidos/ASIN/1555812341/icongroupinterna
- **The Influence of Antibiotics on the Host-Parasite Relationship II** by D. Adam, et al (1986); ISBN: 038715843X; http://www.amazon.com/exec/obidos/ASIN/038715843X/icongroupinterna

- **The Influence of Antibiotics on the Host-Parasite Relationship II** (1986); ISBN: 354015843X; http://www.amazon.com/exec/obidos/ASIN/354015843X/icongroupinterna
- **The Use of Antibiotics** (1987); ISBN: 0397504454; http://www.amazon.com/exec/obidos/ASIN/0397504454/icongroupinterna
- **Topical Application of Antibiotics: Recent Advances in Ophthalmology (Ophthalmologica, Vol 211, Suppl. 1, 1997)** by Yoshihito Honda (Editor), Wolfgang Behrens-Baumann (Editor) (1997); ISBN: 3805564791; http://www.amazon.com/exec/obidos/ASIN/3805564791/icongroupinterna
- **Treatment Modalities in Lung Cancer (Antibiotics and Chemotherapy, Vol 41)** by R. Arriagada, t Le Chevalier (Editor) (1988); ISBN: 3805547757; http://www.amazon.com/exec/obidos/ASIN/3805547757/icongroupinterna
- **Ullmann's Encyclopedia of Industrial Chemistry, Vol. A2: Amines, Aliphatic to Antibiotics** by Hans-Jürgen Arpe (Editor) (1997); ISBN: 3527201025; http://www.amazon.com/exec/obidos/ASIN/3527201025/icongroupinterna
- **Use of Antibiotic Resistance Markers in Genetically Modified Plants for Human Food** by D. C. Burke (Editor) (1996); ISBN: 0756728150; http://www.amazon.com/exec/obidos/ASIN/0756728150/icongroupinterna
- **When Antibiotics Fail Restoring the Ecology of the Body** by Marc Lappe, Michael Schmidt (Introduction) (1995); ISBN: 1556431910; http://www.amazon.com/exec/obidos/ASIN/1556431910/icongroupinterna
- **Workshop on Biotechnology of Antibiotics, Alkaloids and Steroids of Medicinal Importance** by R. Vlahov (1991); ISBN: 0895736535; http://www.amazon.com/exec/obidos/ASIN/0895736535/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 "antibiotics" (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]

- **Antibiotic susceptibility testing by the CDS method: a manual for medical and veterinary laboratories, 2002** Author: Bell, S. M. (Sydney M.); Year: 2003; Randwick, NSW: Dept. of Microbiology, Prince of Wales Hospital, Antibiotic Reference Laboratory, c2002; ISBN: 0958185301

[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**.

- **Antibiotic therapy for staphylococcal diseases, ed. by Henry Welch and Maxwell Finland.** Author: Welch, Henry.; Year: 1955; New York, Medical Encyclopedia [c1959]
- **Antibiotic treatment of venereal diseases.** Author: Luger, Alfred P.; Year: 1965; Basel, New York, Karger, 1968
- **Antibiotics and chemotherapeutic agents in clinical and laboratory practice.** Author: Lorian, Victor.; Year: 1964; Springfield, Ill., Thomas [c1966]
- **Antibiotics in agriculture; proceedings of the fifth symposium of the Group of European Nutritionists in Jouy-en-Josas, April 25-27, 1966. Antibiotiques en agriculture; comptes rendus. Edited by J. C. Somogyi and A. C. François.** Author: Somogyi, J. C. (Johann Carl); Year: 1965; Basel, New York, Karger, 1968
- **Antibiotics in nutrition.** Author: Jukes, Thomas H. (Thomas Hughes),; Year: 1963; New York, Medical Encyclopedia [c1955]
- **Antibiotics in the treatment of genital tuberculosis in women.** Author: Rydén, Åke Bertil Värner,; Year: 2002; Lund, 1950
- **Antibiotics; advances in research, production and clinical use. Proceedings, ed. by Milos Herold and Zdenek Gabriel.** Author: Herold, Milos.; Year: 1964; London, Butterworth, 1966
- **Antibiotics; origin, nature and properties [by] Tadeusz Korzybski [et al.** Author: Korzybski, Tadeusz.; Year: 1964; Oxford, New York, Pergamon Press; Warszawa, Polish Scientific Publishers [1967]
- **Biogenesis of antibiotic substances, edited by Zdenko Vanek and Zdenek Hostálek.** Author: Vanek, Z. (Zdenko); Year: 1965; Prague, Pub. House of the Czechoslovak Academy of Sciences; New York, Academic Press, 1965
- **Index of antibiotics from actinomycetes. Editor-in-chief: Hamao Umezawa. Editors: Shinichi Kondo [et al.].** Author: Umezawa, Hamao.; Year: 2003; Tokyo, University of Tokyo Press; State College, Pa., University Park Press [1967]
- **Influence of some streptomyces antibiotics on the inner ear of the guinea pig; electrophysiological and histological study [by] F. Ostyn and J. Tyberghein.** Author: Ostyn, F.; Year: 1965; Uppsala, 1968
- **Roentgenographic diagnosis of genital tuberculosis in the female and roentgenographic effects of antibiotic therapy. [Tr. from the Swedish].** Author: Ekengren, Kristina.; Year: 2000; Stockholm, 1955
- **The chemistry of the antibiotics used in medicine.** Author: Evans, Ronald Major.; Year: 1963; Oxford, Pergamon Press [1965]
- **The therapeutic use of antibiotics in hospital practice; proceedings of a symposium held at St. Thomas's Hospital Medical School, ed. by Mark Ridley [and] Ian Phillips.** Author: Ridley, Mark,; Year: 1957; Edinburgh, Livingstone, 1966
- **Use of antibiotics and chemotherapeutics in surgery.** Author: Sandusky, William R.,; Year: 1963; Chicago, Year Book Medical Publishers, 1964

## Chapters on Antibiotics

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

- **Prophylactic Antibiotic Use**

  Source: in Newman, M.G. and van Winkelhoff, A.J., eds. Antibiotic and Antimicrobial Use in Dental Practice. 2nd ed. Chicago, IL: Quintessence Publishing Co, Inc. 2001. p. 215-225.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $32.00 plus shipping and handling. ISBN: 0867153970.

  Summary: Antibiotic prophylaxis is the administration of antibiotics to patients who have no known infection for the purpose of preventing microbial colonization and reducing the potential for postoperative complications. This chapter on the use of prophylactic antibiotic use is from a textbook that integrates basic facts and principles of antibiotic therapy with recently emerged concepts of care. The authors outline the principles of antibiotic prophylaxis, then discuss bacteremia (bacteria in the blood) leading to colonization, including dental causes of bacteremia; infective endocarditis (heart infection); premedications; patients with special considerations, including those who are on antibiotics already for dental or medical purposes, patients who require a series of dental procedures over a 9 to 14 day period, and susceptible patients with aggressive periodontitis; and patients with systemic disease, including hemodialysis patients, transplant patients, immunocompromised patients, patients with joint prostheses, and patients with a diminished capacity to fight infection. The authors conclude by stressing that a high level of oral hygiene reduces bacteremia, a fact that should be consistently reiterated to the patient. Important principles, key facts, and clinical insights are highlighted and the chapter concludes with a list of references. 6 figures. 1 table. 22 references.

- **Antibiotics for Oral and Maxillofacial Infections**

  Source: in Newman, M.G. and van Winkelhoff, A.J., eds. Antibiotic and Antimicrobial Use in Dental Practice. 2nd ed. Chicago, IL: Quintessence Publishing Co, Inc. 2001. p. 157-173.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $32.00 plus shipping and handling. ISBN: 0867153970.

  Summary: Infections of the oral and maxillofacial region, although commonly encountered by dentists, can be challenging to manage. This chapter on antibiotics for the treatment of oral and maxillofacial infections is from a textbook that integrates basic facts and principles of antibiotic therapy with recently-emerged concepts of care. The author presents guidelines for using a combination of antibiotics and surgery to manage minor orofacial and odontogenic (arising from the tissues that produce teeth) infections in the office setting. Topics include the microbiology of odontogenic infections; the natural course of odontogenic infections, i.e., cellulitis, abscess, and sinus tract; the spread of infection; the role of depressed host defenses, due to chemotherapy, metabolic diseases, organ transplants, or myeloproliferative diseases; and the use of dental spectrum antibiotics, including penicillin, extended spectrum penicillins,

cephalosporins, erythromycin, clarithromycin, clindamycin, tetracycline, metronidazole, and fluoroquinolones. The author also reviews the principles of therapy, including determination of severity of the infection, evaluation of host defenses, surgical treatment, antibiotic choice, antibiotic administration, follow up, and side effects and secondary infection. The chapter concludes with a discussion of wound infection prophylaxis and special considerations, including sinus perforations, avulsed teeth, osteomyelitis, dry socket (alveolar osteitis), pericoronitis, routine extractions, and impacted third molars (wisdom teeth). Important principles, key facts, and clinical insights are highlighted and the chapter concludes with a list of references. 3 figures. 4 tables. 7 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.

- **Antidiarrheals, Antibiotics, Psychotropics, and Potential New Drug Therapies**

  Source: in Peppercorn, M.A., ed. Therapy of Inflammatory Bowel Disease: New Medical and Surgical Approaches. New York, NY: Marcel Dekker, Inc. 1990. p. 135-144.

  Contact: Available from Marcel Dekker, Inc. P.O. Box 5005, Monticello, NY 12701-5185. (800) 228-1160 or (212) 696-9000. Fax (914) 796-1772. E-mail: bookorders@dekker.com. PRICE: $190.00. ISBN: 0824781694.

  Summary: There are a number of drugs that can be of great use for the individual patient with inflammatory bowel disease (IBD), but whose action is not thought of as directed against IBD itself. There is also an increasing list of agents which appear to have some promise as first-line agents in IBD treatment. This chapter, from a book about the medical and surgical approaches in the management of IBD, discusses antidiarrheals, antibiotics, psychotropics, and potential new drug therapies, and their uses in IBD therapy. The author discusses antidiarrheals, including opiates, cholestyramine, and bulk agents; antibiotics, including sulfasalazine and metronidazole; and psychotropics, including minor tranquilizers and antidepressants. Potential new drug therapies, using agents including sodium cromoglycate, sucralfate, chloroquine,

methotrexate, antituberculous agents, lipoxygenase inhibitors, and immune adjuvants, are discussed. 43 references.

- **Role of Antibiotics in Comfort Care**

  Source: in Olson, E.; Chichin, E.R.; Libow, L.S., eds. Controversies in Ethics in Long-Term Care. New York, NY: Springer Publishing Company. 1996. p. 91-107.

  Contact: Springer Publishing Company. 536 Broadway, New York, NY 10012-9904. (212) 431-4370; FAX (212) 941-7842. PRICE: $34.95 (for the book). ISBN: 0826186009.

  Summary: This book chapter examines the role of antibiotics in comfort care for end-stage dementia patients, and suggests a flexible approach to deciding when to provide or forgo antibiotic therapy. The authors discuss what is meant by comfort care, whether the usual outcomes of antibiotic treatment are consistent with the goals of comfort care, when the use of antibiotics may be considered comfort care, and when the use of antibiotics is more likely to be burdensome. They suggest that the characterization of any treatment option is based on its ability to influence both symptom relief (quality of life) and survival (quantity of life), and propose that antibiotic therapy may be considered comfort care when it is uniquely effective at relieving symptoms. They also present the examples of pneumonia, urinary tract infection, and infected pressure sores to show how the proposed approach to decision making applies to the problem of infection in end-stage dementia patients residing in long-term care facilities. These examples also illustrate how optimal comfort care is achieved when an antibiotic's unique effectiveness is weighed against its potential to prolong life, in comparison with alternative palliative measures. The authors conclude with a proposal for a flexible approach to comfort care that takes into account the patient's premorbid quality of life, the type of infection, and the likely response in terms of both quality and quantity of life. 22 references.

- **Antibiotic-Associated Colitis**

  Source: in Feigin, R.D. and Cherry, J.D., eds. Textbook of Pediatric Infectious Diseases. 4th ed. Volume 1. Philadelphia, PA: W.B. Saunders Company. 1998. p. 601-605.

  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: $315.00. ISBN: 0721664482.

  Summary: This chapter on antibiotic-associated colitis is from a textbook on pediatric infectious diseases. The author notes that Clostridium difficile colonization and infection accounts for 10 to 25 percent of antibiotic-associated diarrhea and is the major cause of antibiotic-associated pseudomembranous colitis. Diarrhea and colitis develop when antibiotics, especially those with a broad spectrum of activity, disturb the bowel flora and allow overgrowth of C. difficile bacteria. Toxin production then leads to inflammation and secretion of fluids from the colon, resulting in watery diarrhea. If inflammation continues and pseudomembranous colitis develops, the diarrhea becomes bloody. Colitis induced by C. difficile has been reported in patients who did not have prior antibiotics, but this is uncommon. The author considers history, etiology and pathogenesis, clinical manifestations, diagnostic considerations, treatment, and prevention mechanisms. In mild cases, discontinuing antibiotics and implementing supportive measures alone will lead to gradual resolution of symptoms. 2 figures. 1 table. 72 references. (AA-M).

- **Antibiotics in Periodontal Therapy**

  Source: in Newman, M.G. and van Winkelhoff, A.J., eds. Antibiotic and Antimicrobial Use in Dental Practice. 2nd ed. Chicago, IL: Quintessence Publishing Co, Inc. 2001. p. 113-126.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $32.00 plus shipping and handling. ISBN: 0867153970.

  Summary: This chapter on antibiotics for the treatment of periodontal disease is from a textbook that integrates basic facts and principles of antibiotic therapy with recently-emerged concepts of care. The authors note that in general, antibiotics are seldom necessary for treatment of gingivitis (gum inflammation) and chronic periodontal diseases. Scaling, root planing, and periodontal surgery (if indicated) are anti-infective measures that may negate the need for antibiotics. The authors discuss conditions that may call for systemic antimicrobial periodontal therapy, the infecting microorganisms, and the use of antibiotics in situations of plaque formation and gingivitis and periodontitis, and the selection of antibiotic regimens in periodontal therapy (single drug regimens, combination antimicrobial therapy, and sequential regimens). Specific drugs covered are penicillins, tetracyclines, minocycline, doxycycline, metronidazole, clindamycin, ciprofloxin, spiramycin, and amoxicillin and clavulanic acid. Important principles, key facts, and clinical insights are highlighted and the chapter concludes with a list of references. 3 figures. 2 tables. 58 references.

- **Is There a Role for Antibiotics in Crohn's Disease?**

  Source: Jewell, D.P.; Warren, B.F.; Mortensen, N.J., eds. Challenges in Inflammatory Bowel Disease. Malden, MA: Blackwell Science, Inc. 2001. p.121-126.

  Contact: Available from Blackwell Science, Inc. 350 Main Street, Commerce Place, Malden, MA 02148. (800) 215-1000 or (617) 388-8250. Fax (617) 388-8270. E-mail: books@blacksci.com. Website: www.blackwell-science.com. PRICE: $145.95. ISBN: 0632051698.

  Summary: This chapter on the role of antibiotics in treating Crohn's disease is from a book that offers an approach to the subject of inflammatory bowel disease (IBD) that highlights current areas of controversy. After a brief introduction, the authors discuss the use of metronidazole, ciprofloxacin, broad-spectrum antibiotics, and antimycobacterial agents. The authors conclude that the role of antibiotics in the treatment of Crohn's disease is not yet well defined. Antibiotics work in perianal disease although controlled trials are lacking. Only metronidazole for the treatment of Crohn's disease has been adequately studied in controlled trials. However, many more good clinical trials are needed, including the comparison of glucocorticosteroids and antibiotics for long-term. The promising results with clarithromycin need confirmation. 1 table. 35 references.

- **Use of Antibiotics and Other Anti-infectious Agents in Ulcerative Colitis**

  Source: in Bayless, T.M. and Hanauer, S.B. Advanced Therapy of Inflammatory Bowel Disease. Hamilton, Ontario: B.C. Decker Inc. 2001. p. 149-151.

  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 the use of antibiotics and other anti infectious agents in ulcerative colitis (UC) 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 UC, together known as inflammatory bowel disease (IBD). Abundant evidence suggests that an imbalance between luminal (in the intestines) bacteria and the host inflammatory and immune response plays a central role in the pathogenesis (development) of inflammatory bowel disease (IBD). Development of UC has been observed after enteric (through the gastrointestinal tract) infection with Salmonella, Shigella, and Yersinia species. While these specific pathogens are not considered etiologic (causative) agents of UC, a transient infection may initiate a cascade of inflammatory events that, in predisposed individuals, can lead to UC. Similarly, although many enteric pathogens have been associated with relapse of UC, there is no evidence that persistence of these infections is a cause of the disease. In recent UC clinical trials, administration of live non-pathogenic Escherichia coli or a mixture of bifidobacteria, lactobacilli, and streptococci was equivalent to mesalamine in maintenance of remission. Taken together, these data suggest that the beneficial effect of antibiotics may not result from a long-term reduction in total bacterial load but rather from a qualitative alteration of the resident bacterial population. The recent human data further suggest a role for probiotics in the maintenance therapy for UC patients. This topic is also discussed in the chapter on the role of bacteria in CD and the chapter on pouchitis. The authors note that the lack of antibiotic benefits in randomized trials should not completely preclude their use in the management of selected UC patients. In clinical practice, these drugs may benefit patients with an acute flare of the disease, toxic patients with or without megacolon, and subsets of patients with refractory disease. 11 references.

# CHAPTER 8. MULTIMEDIA ON ANTIBIOTICS

## Overview

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

- **Prophylactic Antibiotics: Uses and Abuses for Physicians and Dentists**

  Source: Chapel Hill, NC: Health Sciences Consortium. 1992. (videocassette).

  Contact: Available from Health Sciences Consortium (HSC). 201 Silver Cedar Court, Chapel Hill, NC 27514-1517. (919) 942-8731; Fax (919) 942-3689. PRICE: $395.00 plus shipping and handling; HSC members $276.50 plus shipping and handling. Rentals (per title) $80.00; HSC Members $55.00; plus shipping and handling. Previews (per title) $30.00; HSC members $20.00; plus shipping and handling. Order Number D920-VI-008.

  Summary: Dentists give antibiotics before procedures to patients with cardiac valvular and congenital abnormalities in order to prevent bacterial endocarditis. This continuing education videotape program identifies the organisms that cause endocarditis following dental procedures, and reviews current research and recent recommendations concerning prophylactic antibiotic use by dental patients. The program also discusses office protocols to ensure communication between the dentist and physician for optimal care of patients at risk for endocarditis. (AA).

## Bibliography: Multimedia on Antibiotics

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 antibiotics (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 antibiotics:

- **Antibiotic update [videorecording]** Source: Dept. of Medicine, Emory University, School of Medicine; Year: 1978; Format: Videorecording; Atlanta: Georgia Regional Medical Television Network: [for loan and sale by A. W. Calhoun Medical Library], 1978
- **Antibiotics [motion picture]: curative drugs** Source: produced by the Special Educational Services Division of the WGBH Educational Foundation; [presented by] the Lowell Institute in cooperation with Tufts-New England Medical Center; Year: 1967; Format: Motion picture; United States: Tufts-New England Medical Center, c1967
- **Antibiotics in orthopaedics [slide]** Source: American Academy of Orthopaedic Surgeons; Year: 1976; Format: Slide; [Chicago]: The Academy, [1976]
- **Antibiotics in surgery [sound recording]** Source: American College of Surgeons; Year: 1977; Format: Sound recording; [Chicago]: The College, [1977]
- **Antitubercular drugs, broad spectrum antibiotics [videorecording]** Source: Minnesota Video Nursing Education; Year: 1970; Format: Videorecording; [Minneapolis, Minn.]: Minnesota Video Nursing Education; [St. Paul, Minn.: for loan by Telstar Productions, inc.], c1970
- **Impact of dosing regimens on therapeutic efficacy of antibiotics [videorecording]** Source: NCME; Year: 1987; Format: Videorecording; Secaucus, N.J.: Network for Continuing Medical Education, [1987]
- **Indications for prophylactic antibiotics [videorecording]** Source: University of Virginia, School of Medicine; Year: 1976; Format: Videorecording; [Charlottesville]: The University: [for loan or sale by its Medical Center, Audiovisual Center, 1976]
- **Present status of antibiotics in dentistry [motion picture]** Source: presented by Massachusetts Dental Society and Wyeth Laboratories; Year: 1957; Format: Motion picture; United States: The Society: The Laboratories, [1957]
- **Prophylactic antibiotics [videorecording]: which, when, how to use.** Year: 1985; Format: Videorecording; New York: Network for Continuing Medical Education, [1985]
- **Prophylactic use of antibiotics in gynecology [videorecording]** Source: Academy of Health Sciences; Year: 1975; Format: Videorecording; Fort Sam Houston, Tex.: The Academy: [for loan by its Health Sciences Media Division, 1975]
- **Prophylactic use of antibiotics in obstetrics [videorecording]** Source: Academy of Health Sciences; Year: 1975; Format: Videorecording; Fort Sam Houston, Tex.: The Academy: [for loan by its Health Sciences Media Division, 1975]
- **Salmonellosis, shigellosis and antibiotics [videorecording]** Source: Emory University School of Medicine; Year: 1975; Format: Videorecording; Atlanta: Georgia Regional Medical Television Network: [for loan or sale by A. W. Calhoun Medical Library], 1975
- **Surgical infections and antibiotics [sound recording]** Source: American College of Surgeons; Year: 1976; Format: Sound recording; Chicago: The College, p1976

- **The new antibiotics [videorecording]: when are they indicated?** Year: 1983; Format: Videorecording; New York: Network for Continuing Medical Education, 1983
- **The Use and abuse of antibiotics in the surgery of trauma [sound recording]** Source: American College of Surgeons; Year: 1976; Format: Sound recording; Chicago: The College, p1976
- **The Use of antibiotics in the emergency room [sound recording]** Source: Illinois Chapters of the American College of Emergency Physicians and the Emergency Department Nurses Association; produced by Teach'em; Year: 1976; Format: Sound recording; Chicago: The Chapters: [for sale by Teach'em], 1976
- **Time factors in antibiotic effectiveness [motion picture]** Source: a Pragmaton production, a division of Frank J. Corbett, Inc; Year: 1977; Format: Motion picture; [United States]: Beecham Laboratories, c1977
- **When to use which antibiotic for what [sound recording]** Source: American College of Physicians; produced by Audio-Digest Foundation; Year: 1976; Format: Sound recording; Glendale, Calif.: The Foundation, p1976

# CHAPTER 9. PERIODICALS AND NEWS ON ANTIBIOTICS

## Overview

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

## News Services and Press Releases

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

- **Short course of antibiotic therapy suitable for ventilator-associated pneumonia**
  Source: Reuters Industry Breifing
  Date: November 19, 2003
- **HIV infection predisposes to antibiotic allergies**
  Source: Reuters Medical News
  Date: November 12, 2003

- **Japan's Sankyo licences Roche for new antibiotic**
  Source: Reuters Industry Breifing
  Date: November 10, 2003
- **Community E. coli isolates have high resistance rate to usual first-line antibiotic**
  Source: Reuters Medical News
  Date: October 28, 2003
- **U.S. outlines steps to study animal antibiotic risk**
  Source: Reuters Industry Breifing
  Date: October 23, 2003
- **Sulfonamide antibiotics do not cross react with other sulfa drugs**
  Source: Reuters Industry Breifing
  Date: October 22, 2003
- **Genzyme diarrhea drug takes longer than antibiotic**
  Source: Reuters Industry Breifing
  Date: October 20, 2003
- **Fermented milk shown to prevent antibiotic-induced diarrhea in children**
  Source: Reuters Medical News
  Date: October 14, 2003
- **Study: Antibiotics may help stave off Alzheimer's**
  Source: Reuters Industry Breifing
  Date: October 09, 2003
- **Community-acquired antibiotic-resistant infections increasingly common**
  Source: Reuters Industry Breifing
  Date: October 09, 2003
- **Antibiotics may slow Alzheimer's-related cognitive decline**
  Source: Reuters Medical News
  Date: October 09, 2003
- **U.S. warns AstraZeneca on antibiotic promotion**
  Source: Reuters Industry Breifing
  Date: October 06, 2003
- **Infants treated with antibiotics at increased risk for atopy and asthma**
  Source: Reuters Medical News
  Date: September 30, 2003
- **Dramatic increase seen in antibiotic-resistant gut bacteria**
  Source: Reuters Medical News
  Date: September 16, 2003
- **Bayer licenses antibiotic from Paratek**
  Source: Reuters Industry Breifing
  Date: September 16, 2003
- **FDA approves new cyclic lipopeptide antibiotic by Cubist Pharma**
  Source: Reuters Industry Breifing
  Date: September 15, 2003
- **Bristol-Myers sells back rights to antibiotic**
  Source: Reuters Industry Breifing
  Date: September 02, 2003

- **Antibiotic use has declined among U.S. children**
  Source: Reuters Medical News
  Date: September 02, 2003
- **Antibiotic use drops among US children**
  Source: Reuters Industry Breifing
  Date: September 02, 2003
- **Publicly insured children in U.S. with sickle cell disease not getting needed antibiotics**
  Source: Reuters Medical News
  Date: August 27, 2003
- **Antibiotic use tied to reduced stroke risk**
  Source: Reuters Industry Breifing
  Date: August 07, 2003
- **Sixty days of antibiotics may not be enough after anthrax exposure**
  Source: Reuters Industry Breifing
  Date: July 28, 2003
- **Empiric antibiotic therapy for pharyngitis not cost effective**
  Source: Reuters Medical News
  Date: July 15, 2003
- **Antibiotic therapy for 3 days suitable for premature rupture of membranes**
  Source: Reuters Medical News
  Date: July 08, 2003
- **Antibiotic treatment does not alter the natural history of reactive arthritis**
  Source: Reuters Medical News
  Date: July 04, 2003
- **Cubist starts phase I trial of new antibiotic**
  Source: Reuters Industry Breifing
  Date: June 24, 2003
- **Vicuron acne antibiotic shows promise in phase I**
  Source: Reuters Industry Breifing
  Date: June 18, 2003
- **Apotex to sell Orchid's (ORCD.BO) antibiotics in US**
  Source: Reuters Industry Breifing
  Date: June 02, 2003

### The NIH

Within MEDLINEplus, the NIH has made an agreement with the New York Times Syndicate, the AP News Service, and Reuters to deliver news that can be browsed by the public. Search news releases at **http://www.nlm.nih.gov/medlineplus/alphanews_a.html**. MEDLINEplus allows you to browse across an alphabetical index. Or you can search by date at the following Web page: **http://www.nlm.nih.gov/medlineplus/newsbydate.html**. Often, news items are indexed by MEDLINEplus within its search engine.

### Business Wire

Business Wire is similar to PR Newswire. To access this archive, simply go to **http://www.businesswire.com/**. You can scan the news by industry category or company name.

### Market Wire

Market Wire is more focused on technology than the other wires. To browse the latest press releases by topic, such as alternative medicine, biotechnology, fitness, healthcare, legal, nutrition, and pharmaceuticals, access Market Wire's Medical/Health channel at **http://www.marketwire.com/mw/release_index?channel=MedicalHealth**. Or simply go to Market Wire's home page at **http://www.marketwire.com/mw/home**, type "antibiotics" (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 "antibiotics" (or synonyms). If you know the name of a company that is relevant to antibiotics, 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 "antibiotics" (or synonyms).

## Newsletters on Antibiotics

Find newsletters on antibiotics 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 "antibiotics." 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 "antibiotics" (or synonyms) into the "For these words:" box. The following list was generated using the options described above:

- **Overused Antibiotics Lead to Resistant UTIs: Assessing Resistance Risk, Testing Fluoroquinolone Alternatives Key**

  Source: Urology Times. 22(3): 2. March 1994.

Contact: Available from Advanstar Communications, Inc. Corporate and Editorial Offices, 7500 Old Oak Boulevard, Cleveland, OH 44130. (216) 243-8100.

Summary: This brief news article, from a professional newsletter, warns that physicians' overuse of fluoroquinolones to treat urinary tract infections (UTIs) has led to a significant increase in ciprofloxacin-resistant Escherichia coli. Topics include problems with recurrence of urinary tract infections; recent increases in the use of fluoroquinolones; risk factors for ciprofloxacin-resistant E coli UTIs; experience with 54 patients with resistant UTIs; and the course of ciprofloxacin-resistant E coli-induced UTIs. The article concludes with a brief discussion of alternative treatments, including the combination of amoxicillin and potassium clavulanate.

## 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 "antibiotics" (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 antibiotics:

- **Antibiotics for Kids: Overprescribed?**

  Source: HealthNews. 2(16): 3. November 19, 1996.

  Contact: Available from HealthNews. P.O. Box 52924, Boulder, CO 80322-2924. (800) 848-9155 or (617) 893-3800; E-mail: hnews@world.std.com.

  Summary: This brief newsletter article reviews the use of antibiotics for children, most notably to combat ear infections (otitis media). The author reports on a study that investigated the proportion of infants who had received antibiotics in their first 6 months of life. By 3 months of age, 27 percent of the babies (total number was 789 children) had been given at least one antibiotic; by 6 months of age, that figure was up to 70 percent. Amoxicillin was the most frequently prescribed drug in this group of babies. The author describes why it may be good to avoid such extensive use of antibiotics. The author also offers some practical suggestions for parents dealing with a suspected ear infection in their infant. The author notes that some parents and doctors may decide together to carefully watch ear infections in babies older than 2 or 3 months and to hold off on antibiotics for the first 48 to 72 hours, the time in which most children will get better by themselves. 1 figure.

- **Use of Antibiotics in Periodontal Therapy**

  Source: Oral Care Report. 11(4): 5,8. 2001.

  Contact: Available from Oral Care Report. c/o Dr. Chester W. Douglass, Department of Oral Health Policy, Harvard School of Dental Medicine, 188 Longwood Avenue, Boston, MA 02115. Fax (617) 432-0047. E-mail: colgateoralcarereport@hms.harvard.edu. Website: www.colgateprofessional.com (full-text available online).

  Summary: This brief report reviews the use of antibiotics in periodontal therapy. Treatment of periodontitis is based on four scientific principles: that bacteria cause the

disease; the disease is chronic in nature; clinicians cannot remove all plaque and calculus on infected root surfaces; and the disease is recurrent and cannot be cured. Clinical research has shown that scaling and root planing (SRP) combined with systemic antibiotic administration was more effective than SRP alone in certain patient groups and with particular forms of periodontitis. This article summarizes the outcome of trials with either tetracycline, Augmentin, clindamycin, or metronidazole. The author also outlines the potential adverse effects of systemic antibiotics and the development of antibiotic resistance. The author notes that given the varied success of antibiotic treatment for periodontitis, together with the concerns regarding antibiotic resistance, local delivery of antimicrobials offers a new strategy in the treatment of adult periodontitis for certain patient subgroups that do not respond favorably to conventional therapy alone. Local delivery of antibiotics offers the advantages of direct access to the site of periodontitis, a therapeutic level that is above the minimum inhibitory concentration, and a minimal uptake of the drug into the systemic circulation, which reduces side effects and drug interactions. 1 figure. 3 references.

## Academic Periodicals covering Antibiotics

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

**Antipyrine and Benzocaine**

- **Otic - U.S. Brands:** Allergen; Antiben; Auralgan; Aurodex; Auroto; Dolotic; Otocalm
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202066.html

**Aztreonam**

- **Systemic - U.S. Brands:** Azactam
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202078.html

**Cephalosporins**

- **Systemic - U.S. Brands:** Ancef; Ceclor; Ceclor CD; Cedax; Cefadyl; Cefizox; Cefobid; Cefotan; Ceftin; Cefzil; Ceptaz; Claforan; Duricef; Fortaz; Keflex 20; Keftab 20; Kefurox; Kefzol; Mandol; Maxipime; Mefoxin; Monocid; Omnicef; Rocephin; Suprax; Tazicef; Tazidime; Vantin; Velo
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202119.html

**Chloramphenicol**

- **Systemic - U.S. Brands:** Chloromycetin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202127.html

**Clindamycin**

- **Topical - U.S. Brands:** Clinda-Derm
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202146.html

**Cycloserine**

- **Systemic - U.S. Brands:** Seromycin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202175.html

**Dornase Alfa**

- **Inhalation - U.S. Brands:** Pulmozyme
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202710.html

**Doxycycline**

- **Dental - U.S. Brands:** Atridox
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203716.html

**Doxycycline for Dental Use**

- **Systemic - U.S. Brands:** Periostat
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203724.html

**Erythromycin**

- **Ophthalmic - U.S. Brands:** Ilotycin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202220.html

**Erythromycin and Sulfisoxazole**

- **Systemic - U.S. Brands:** Eryzole; Pediazole
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202224.html

**Fosfomycin**

- **Systemic - U.S. Brands:** Monurol
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203522.html

**Gentamicin**

- **Ophthalmic - U.S. Brands:** Garamycin; Gentacidin; Gentafair; Gentak; Ocu-Mycin; Spectro-Genta
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202604.html
- **Topical - U.S. Brands:** Garamycin; Gentamar; G-Myticin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202258.html

**Kanamycin**

- **Oral - U.S. Brands:** Kantrex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202312.html

**Lansoprazole**

- **Systemic - U.S. Brands:** Prevacid
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202787.html

**Lincomycin**

- **Systemic - U.S. Brands:** Lincocin; Lincorex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202328.html

**Linezolid**

- **Systemic - U.S. Brands:** Zyvox
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500165.html

**Metronidazole**

- **Systemic - U.S. Brands:** Flagyl; Protostat
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202365.html

**Mometasone**

- **Nasal - U.S. Brands:** Nasonex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203589.html

**Neomycin**

- **Topical - U.S. Brands:** Myciguent
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202397.html

**Neomycin, Polymyxin B, and Bacitracin**

- **Ophthalmic - U.S. Brands:** Neotal; Ocu-Spor-B; Ocusporin; Ophthalmic; Spectro-Sporin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202399.html

- **Topical - U.S. Brands:** Foille; Mycitracin; Topisporin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202400.html

**Neomycin, Polymyxin B, and Gramicidin**

- **Ophthalmic - U.S. Brands:** Ocu-Spor-G; Tribiotic; Tri-Ophthalmic
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202401.html

**Neomycin, Polymyxin B, and Hydrocortisone**

- **Otic - U.S. Brands:** Cort-Biotic; Cortisporin; Cortomycin; Drotic; Ear-Eze; LazerSporin-C; Octicair; Octigen; Otic-Care; Otimar; Otisan; Otocidin; Otocort; Pediotic
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202403.html

**Norfloxacin**

- **Ophthalmic - U.S. Brands:** Chibroxin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202635.html

**Ofloxacin**

- **Ophthalmic - U.S. Brands:** Ocuflox
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202687.html

**Omeprazole**

- **Systemic - U.S. Brands:** Prilosec
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202423.html

**Penicillins**

- **Systemic - U.S. Brands:** Amoxil; Bactocill; Beepen-VK; Betapen-VK; Bicillin L-A; Cloxapen; Crysticillin 300 A.S.; Dycill; Dynapen; Geocillin; Geopen; Ledercillin VK; Mezlin; Nafcil; Nallpen; Omnipen; Omnipen-N; Pathocil; Pen Vee K; Pentids; Permapen; Pfizerpen; Pfizerpen-AS; Pi
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202446.html

**Phenazopyridine**

- **Systemic - U.S. Brands:** Azo-Standard; Baridium; Eridium; Geridium; Phenazodine; Pyridiate; Pyridium; Urodine; Urogesic; Viridium
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202455.html

**Probenecid**

- **Systemic - U.S. Brands:** Benemid; Probalan
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202480.html

**Quinupristin and Dalfopristin**

- **Systemic - U.S. Brands:** Synercid
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500048.html

**Rifampin and Isoniazid**

- **Systemic - U.S. Brands:** Rifamate
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202512.html

**Sparfloxacin**

- **Systemic - U.S. Brands:** Zagam
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203530.html

**Tetracyclines**

- **Topical - U.S. Brands:** Achromycin; Aureomycin; Meclan; Topicycline
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202553.html

**Tobramycin and Dexamethasone**

- **Ophthalmic - U.S. Brands:** Tobradex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203776.html

**Vancomycin**

- **Oral - U.S. Brands:** Vancocin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202589.html
- **Systemic - U.S. Brands:** Vancocin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202590.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 antibiotics 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 "antibiotics" (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 antibiotics:

- **Bacitracin (trade name: Altracin)**

  http://www.rarediseases.org/nord/search/nodd_full?code=568

- **Filgrastim (trade name: Neupogen)**

  http://www.rarediseases.org/nord/search/nodd_full?code=800

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[12]:

- 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/**

[12] 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.[13] 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:[14]

- **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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[13] 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**).

[14] 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 "antibiotics" 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 "antibiotics" (or synonyms) into the "For these words:" box. The following is a sample result:

- **Transcript: Oral Aspects of Behcet's from the 1994 American Behcet's Disease Association (ABDA) Patient Family Conference**

  Source: Minneapolis, MN: American Behcet's Disease Association (ABDA). 1994. 31 p.

  Contact: Available from American Behcet's Disease Association (ABDA). P.O. Box 6663, Minneapolis, MN 55406-0663. (612) 722-9554; Fax (612) 722-2218. PRICE: $6.00 each.

  Summary: This document is a transcript of Dr. James J. Sciubba's address at the 1994 American Behcet's Disease Association (ABDA) Patient Family Conference. Dr. Sciubba spoke on the oral aspects of Behcet's disease. The presentation focused on the aphthous ulcers (canker sores) and other clinical lesions that occur in people with Behcet's disease. The speech was illustrated by a series of slides depicting the oral lesions. Dr. Sciubba refers to these slides in his talk. Topics include the locations of oral lesions, the etiology of aphthous ulcers, the three types of canker sores, the clinical presentation of these ulcers, treatment options (cauterization, topical steroids, **antibiotics,** diet modification, intralesional therapy), the criteria for Behcet's disease, and drug therapy (steroids, methotrexate, cyclosporin, interferons, FK506, thalidomide). The transcript also includes a question and answer session between Dr. Sciubba and the audience.

- **Prevention and Management of Urinary Tract Infections Among People with Spinal Cord Injuries: January 27-29, 1992: Resource Papers**

  Source: Washington, DC: National Institute on Disability and Rehabilitation Research. 1992. 105 p.

  Contact: Available from National Institute on Disability and Rehabilitation Research. Department of Education, 600 Independence Avenue SW, Washington, DC 20202. (202) 205-9184. PRICE: Single copy free.

  Summary: This document reprints the papers from a conference on the prevention and management of urinary tract infections (UTI) among people with spinal cord injuries, held in January of 1992. Ten papers are included, covering topics including the treatment of UTI in patients with spinal cord injury (SCI); vocational implications of UTI; self-diagnosis and management of UTI; definitions for critical terms for discussing

UTI in this population; the psychosocial implications of a neurogenic bladder in SCI; the relationship of drainage method to recommended treatment; prophylactic **antibiotics** and acidification of urine to prevent UTI; the microbiology of UTI; and the potential contribution of urodynamics and imaging studies. Each paper includes numerous references.

- **HIV Treatment Strategy, Part III: Drug Information for People Living With AIDS**

  Contact: Carl Vogel Center, 1012 14th St NW Ste 707, Washington, DC, 20005, (202) 638-0750.

  Summary: This paper provides prescriptive drug treatment information for Persons With AIDS (PWA's). It is important for HIV-positive individuals to talk to a physician about a complete antiviral, immunomodulatory, and prophylactic drug program. Antivirals/antibiotics include AZT, ddc, and/or ddi; Combination of the three is thought to increase overall effectiveness. D4T either alone or with ddi looks promising. Many physicians include acyclovir to prevent HIV activation by herpes viruses. Some physicians recommend IV Compound Q for individuals with CD-4's over 100. Doxycycline is used as an anti-mycoplasma agent, Peptide-T seems most useful for neuropathy and cognitive dysfunction problems. Bitter melon is being tried with CD-4 increases is also looking promising. Some immune modulators include: Antioxidants, antabuse/disulfiram, coenzyme Q10, DNCB, glutathione, isoprinosine, naltrexone, pentoxifylline/trental, recombinant gp 160 vaccine, and thymus derivatives. Pap smears and vaginal exams should be conducted regularly for women. Extra nutrients for women should be implemented.

### The NLM Gateway[15]

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.[16] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "antibiotics" (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 | 247866 |
| Books / Periodicals / Audio Visual | 2589 |
| Consumer Health | 1016 |
| Meeting Abstracts | 3187 |
| Other Collections | 31 |
| Total | 254689 |

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

[16] 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).

### HSTAT[17]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[18] 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.[19] Simply search by "antibiotics" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

### Coffee Break: Tutorials for Biologists[20]

Coffee Break is a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. Here you will find a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[21] 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.[22] This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for

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

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

[19] 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.

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

[21] 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.

[22] 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.

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/**.

# 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 antibiotics 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 antibiotics. 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 antibiotics. 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 "antibiotics":

- Other guides

  **Anthrax**
  http://www.nlm.nih.gov/medlineplus/anthrax.html

  **Bacterial Infections**
  http://www.nlm.nih.gov/medlineplus/bacterialinfections.html

  **Peptic Ulcer**
  http://www.nlm.nih.gov/medlineplus/pepticulcer.html

  **Sinusitis**
  http://www.nlm.nih.gov/medlineplus/sinusitis.html

  **Streptococcal Infections**
  http://www.nlm.nih.gov/medlineplus/streptococcalinfections.html

Within the health topic page dedicated to antibiotics, the following was listed:

- General/Overviews

  **Antibiotic Safety**
  http://www.apic.org/iicw/2002/IICW2002AntibioticSafety.pdf

  **Antibiotics: When They Can and Can't Help**
  Source: American Academy of Family Physicians
  http://familydoctor.org/handouts/680.html

  **Using Antibiotics Sensibly**
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=FL00075

- Treatment

  **Central Venous Access Catheters (CVAC) and Gastrostomy (Feeding) Tubes**
  Source: Society of Interventional Radiology
  http://www.sirweb.org/patPub/venousAccessCatheters.shtml

  **Vascular Access Procedures**
  Source: American College of Radiology, Radiological Society of North America
  http://www.radiologyinfo.org/content/interventional/vascular-access.htm

- Specific Conditions/Aspects

  **Antibiotic-Associated Diarrhea**
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=DS00454

  **Antibiotics: Why Don't They Work on Viral Infections?**
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=HQ01610

  **Antimicrobial Resistance**
  Source: National Institute of Allergy and Infectious Diseases
  http://www.niaid.nih.gov/factsheets/antimicro.htm

**Battle of the Bugs: Fighting Antibiotic Resistance**
Source: Food and Drug Administration
http://www.fda.gov/fdac/features/2002/402_bugs.html

**JAMA Patient Page: Coughs, Colds and Antibiotics**
Source: American Medical Association
http://www.medem.com/medlb/article_detaillb.cfm?article_ID=ZZZAFHOC8GD&sub_cat=277

**Penicillin Allergy**
Source: Mayo Foundation for Medical Education and Research
http://www.mayoclinic.com/invoke.cfm?id=HQ01195

**Risks of Stockpiling Antibiotics to Counter Bioterrorism**
Source: Alliance for the Prudent Use of Antibiotics
http://www.tufts.edu/med/apua/News/Articles/risksOfStockpiling.html

- Children

**Danger of Antibiotic Overuse**
Source: Nemours Foundation
http://kidshealth.org/parent/general/sick/antibiotic_overuse.html

**Your Child & Antibiotics**
Source: Centers for Disease Control and Prevention
http://www.cdc.gov/antibioticresistance/files/html_versions/Your%2520Child%2520and%2520Antibiotics.htm

- Latest News

**HHS, Public Health Partners Unveil New Campaign to Promote Awareness of Proper Antibiotic Use**
Source: 09/17/2003, Centers for Disease Control and Prevention
http://www.cdc.gov/od/oc/media/pressrel/r030917.htm

**More News on Antibiotics**
http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/alphanews_a.html#Antibiotics

**Putting a Chill on Important Pills: Antibiotics Can't Cure Colds And Flus - And Overuse Puts All of US at Risk**
Source: 11/10/2003, New York Times Syndicate
http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory_14587.html

**Researchers Find Possible New Antibiotic**
Source: 10/23/2003, Reuters Health
http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory_14398.html

**U.S. Outlines Steps to Study Animal Antibiotic Risk**
Source: 10/23/2003, Reuters Health
http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory_14402.html

- Men

  **Birth Control Pills: Can Antibiotics Decrease Their Effectiveness?**
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=AN00099

- Organizations

  **Centers for Disease Control and Prevention**
  http://www.cdc.gov/

  **Food and Drug Administration**
  http://www.fda.gov/

  **National Institute of Allergy and Infectious Diseases**
  http://www.niaid.nih.gov/

- Prevention/Screening

  **What Can Be Done about Antibiotic Resistance?**
  Source: Alliance for the Prudent Use of Antibiotics
  http://www.tufts.edu/med/apua/Q&A/Q&A_action.html

- Research

  **Changing Use of Antibiotics in Community-Based Outpatient Practice, 1991--1999**
  Source: American College of Physicians
  http://www.annals.org/cgi/content/full/138/7/I-24

  **Linezolid**
  Source: American College of Physicians
  http://www.annals.org/cgi/content/full/138/2/I-44

  **Reduced: Unnecessary Antibiotics for Children**
  Source: National Institute on Deafness and Other Communication Disorders
  http://www.nidcd.nih.gov/news/releases/02/6_25_02.asp

  **Research Brief: Studies of Iron-Pumping Bacteria May Lead to New Antibiotics**
  Source: National Institute of General Medical Sciences
  http://www.nigms.nih.gov/news/releases/brief_vanderhelm.html

  **Tiny Nanotubes as New Antibiotics**
  Source: National Institute of General Medical Sciences
  http://www.nigms.nih.gov/news/releases/brief_ghadiri.html

- Women

  **Birth Control Pills: Can Antibiotics Decrease Their Effectiveness?**
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=AN00099

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 antibiotics. 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:

- **Help on the Way: Antibiotics**

  Source: Santa Cruz, CA: ETR Associates. 1997. [4 p.].

  Contact: Available from ETR Associates. 4 Carbonero Way, Scotts Valley, CA 95066-4200. (800) 321-4407. Fax (800) 435-8433. Website: www.etr.org. PRICE: Single copy free; $16.00 for 50 copies, discounts for larger orders.

  Summary: This brochure explains how antibiotics work, how they are used, the problem of antibiotic resistance, and treatment options for resistant bacterial infections. Most antibiotics are discovered in fungi. Fungi produce antibiotics because they compete with all kinds of bacteria for food; antibiotics kill bacteria cells, but not other types of cells. Antibiotics sometimes have side effects. These side effects may include mild nausea or diarrhea, greater risk of yeast infections, or increased sensitivity to the sun. The brochure outlines symptoms that indicate a call to a health care provider is necessary, including a cut that becomes swollen, tender, hot, or red; any injury that develops red streaks extending from it; a puncture wound or very deep or dirty cut; an illness that starts as a cold or flu and develops these symptoms: a cough with pain in the chest, a fever of 101 degrees that persists for more than 2 days, a sore throat that lasts more than 3 days, sinus pressure with dark mucus that does not improve within 5 days, ear pain that worsens or lasts more than a few days, severe headache with fever, or symptoms that worsen after starting to get better. One sidebar explains how resistance happens: some bacteria cells have an extra loop of genes called a plasmid; plasmids carry genes that allow the bacteria to survive exposure to antibiotics. The author cautions that bacteria that are resistant to antibiotics can arise partly due to patients ending treatment too soon. Strains of tuberculosis, gonorrhea, and pneumonia have developed resistance to antibiotics. The brochure also outlines strategies to avoid problems when taking antibiotics, the differences between viruses and bacteria, and guidelines for the administration and use of antibiotics. 1 figure.

- **Your Child and Antibiotics: Unnecessary Antibiotics CAN Be Harmful**

  Source: Elk Grove Village, IL: American Academy of Pediatrics (AAP). 1997. [2 p.].AV.Available from American Academy of Pediatrics (AAP). 141 Northwest Point Boulevard, Elk Grove Village, IL 60007-1098. (800) 433-9016 (members) or (888) 227-1773 (nonmembers). Fax (847) 434-8000. Website: www.aap.org. PRICE: $24.95 per 100 copies (100 copies minimum); $29.95 per 100 copies (non-members).

  Contact: Available from American Academy of Pediatrics. Division of Publications, 141 Northwest Point Boulevard, P.O. Box 927, Elk Grove Village, IL 60009-0927. (800) 433-

9016 or (847) 228-5005; Fax (847) 228-1281; http://www.aap.org. PRICE: $24.95 per 100 copies (100 copies minimum); $29.95 per 100 copies (non-members).

Summary: This brochure from the American Academy of Pediatrics informs parents about the over-use of antibiotics, the potential for antibiotic-resistant bacteria strains to develop, and how to determine when antibiotics are needed and when they are not. The brochure stresses that repeated and improper use of antibiotics are some of the main causes of the increase in resistant bacteria. Some of these resistant bacteria can be treated with more powerful medicines, which may need to be given intravenously in the hospital, and a few resistant bacteria are already untreatable. The brochure lists common diagnoses and the likelihood that antibiotics are indicated. These include ear infections, sinus infections, cough or bronchitis, sore throat, and colds. Although viral infections may sometimes lead to bacterial infections, treating viral infections with antibiotics to prevent bacterial infections does not work, and may lead to infection with resistant bacteria. The brochure concludes with the answers to a brief list of commonly asked questions. The brochure is illustrated with full-color photographs of children.

- **Antibiotics Before Dental Treatment: Preventing Bacterial Endocarditis**

  Source: JADA. Journal of the American Dental Association. 133(1): 127. January 2002.

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

  Summary: This fact sheet familiarizes readers with the use of antibiotics before dental treatment as a strategy to prevent bacterial endocarditis (a bacterial infection of the heart valves or tissues). Any time there is bleeding in the mouth, oral bacteria can enter the bloodstream and travel to the heart. This presents a risk for some patients who have cardiac abnormalities or other heart conditions. Premedication (taking antibiotics before the treatment) may be necessary for dental procedures such as professional tooth cleaning, extractions, incision and drainage of infected oral tissue, some types of injections, and some oral surgeries. The fact sheet lists the indications for the use of premedication and encourages readers to tell their dentists about any change in their own health status. The fact sheet concludes by reminding readers of the importance of regular, adequate daily dental hygiene.

- **Antibiotics**

  Source: Canadian Journal of Gastroenterology. 12(6): 390-391. September 1998.

  Contact: Available from Pulsus Group, Inc. 2902 South Sheridan Way, Oakville, Ontario, Canada L6J 7L6. (905) 829-4770. Fax (905) 829-4799. E-mail: pulsus@pulsus.com.

  Summary: This fact sheet for patients is printed in a physician's gastroenterology journal and summarizes the use of antibiotics in bowel disease, including potential side effects. Antibiotics are not first line therapy for inflammatory bowel disease (IBD) but are often given in addition to other medications, particularly for Crohn's disease. They are most often used to treat perineal disease (abscesses and fistulas in the perineum). However, antibiotics may also be useful in fighting disease in other parts of the intestine and helping prevent recurrence after surgery for Crohn's disease. The most commonly prescribed antibiotics for IBD are metronidazole and ciprofloxacin. Some of the more common side effects of metronidazole are nausea, diarrhea, abdominal pain, metallic taste, and a sore tongue. Metronidazole may increase the effects of other drugs as well, particularly lithium and warfarin. The most frequent side effects of ciprofloxacin are nausea, vomiting, skin rash, diarrhea, and headache. Also, ciprofloxacin may increase

the effects of theophylline and caffeine. Both metronidazole and ciprofloxacin have the potential to cause oral thrush (fungal infection of the mouth). The fact sheet concludes that, although it seems as if there are a number of side effects, most patients do well on these drugs and have no problems.

### 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 "antibiotics" (or synonyms). The following was recently posted:

- **Antibiotic prophylaxis in surgery. A national clinical guideline**

  Source: Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]; 2000 July; 36 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2911&nbr=2137&string=antibiotics

- **Practice management guidelines for prophylactic antibiotic use in open fractures**

  Source: Eastern Association for the Surgery of Trauma - Professional Association; 2000; 28 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2675&nbr=1901&string=antibiotics

- **Practice management guidelines for prophylactic antibiotic use in penetrating abdominal trauma**

  Source: Eastern Association for the Surgery of Trauma - Professional Association; 2000; 33 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2677&nbr=1903&string=antibiotics

- **Practice management guidelines for prophylactic antibiotic use in tube thoracostomy for traumatic hemopneumothorax**

  Source: Eastern Association for the Surgery of Trauma - Professional Association; 2000; 16 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2678&nbr=1904&string=antibiotics

- **Practice parameters for antibiotic prophylaxis to prevent infective endocarditis or infective prosthesis during colon and rectal endoscopy**

  Source: American Society of Colon and Rectal Surgeons - Medical Specialty Society; 2000; 8 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2595&nbr=1821&string=antibiotic

- **Principles of appropriate antibiotic use for acute pharyngitis in adults**

  Source: American College of Physicians - Medical Specialty Society; 2001 March 20; 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2744&nbr=1970&string=antibiotics

- **Principles of appropriate antibiotic use for acute sinusitis in adults**

  Source: American College of Physicians - Medical Specialty Society; 2001 March 20; 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2743&nbr=1969&string=antibiotics

- **Principles of appropriate antibiotic use for treatment of acute bronchitis in adults**

  Source: American College of Physicians - Medical Specialty Society; 2001 March 20; 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2745&nbr=1971&string=antibiotics

- **Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults**

  Source: American College of Physicians - Medical Specialty Society; 2001 March 20; 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2742&nbr=1968&string=antibiotics

- **Use of antibiotics in adults**

  Source: Singapore Ministry of Health - National Government Agency [Non-U.S.]; 2000 April; 78 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3434&nbr=2660&string=antibiotics

- **Use of antibiotics in paediatric care**

  Source: Singapore Ministry of Health - National Government Agency [Non-U.S.]; 2002 March; 109 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3436&nbr=2662&string=antibiotics

### 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:

- **Antibiotic Resistance**

  Source: Federation of Chinese American and Chinese Canadian Medical Societies

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7269

- **Antibiotic Resistance: Educational Tools**

  Summary: The tools provided here are designed to help you learn about antibiotic resistance and appropriate antibiotic use in upper respiratory infections.

  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=7694

- **Background on Antibiotic Resistance**

  Summary: Overuse of antibiotics is jeopardizing the usefulness of essential drugs. Decreasing inappropriate antibiotic use is the best way to control resistance.

  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=7693

- **Bacterial Resistance: When Antibiotics Don't Work**

  Summary: A consumer health guide designed to help you understand the problem of bacterial resistance. This guide also contains advice on what you can do to prevent bacterial resistance.

  Source: National Consumers League

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=5433

- **CDC Responds: Treatment Options for Postal and Other Workers Exposed to Anthrax (December 21, 2001)**

  Summary: This broadcast provides new information for treatment options for prevention of inhalation anthrax for persons who were exposed to spores and are completing 60-day courses of prophylactic antibiotics.

  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=6429

- **CDC Responds: Update on Options for Preventive Treatment for Persons at Risk for Inhalational Anthrax (December 21, 2001)**

  Summary: This broadcast provides new information for treatment options for prevention of inhalation anthrax for persons who were exposed to spores and are completing 60-day courses of prophylactic antibiotics.

  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=6430

- **Common Antibiotics**

  Summary: A listing of common antibiotics, including penicillins, sulfonamides, urinary antibacterial agents, and anti-tuberculosis agent, by generic name, trade name and type.

  Source: Alliance for the Prudent Use of Antibiotics

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=2848

- **Doxycycline and Penicillin G Procaine for Inhalational Anthrax (Post-Exposure)**

  Summary: This drug information sheet from FDA's Center for Drug Evaluation and Research provides recommendations for the antibiotics doxycycline and penicillin G procaine for treatment of inhalational anthrax.

  Source: Center for Drug Evaluation and Research, U.S. Food and Drug Administration

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6368

- **Get Smart: Know When Antibiotics Work**

  Summary: Here you can find general information about antibiotic resistance and how to prevent it. You will also find helpful information about colds, the flu, and other illnesses.

  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=7766

- **Statement by the Department of Health and Human Services Regarding Additional Options for Preventive Treatment for Those Exposed to Inhalational Anthrax**

  Summary: Many of those who were exposed to inhalational anthrax in the recent mail attacks are presently concluding their 60-day course of preventive antibiotic treatment.

  Source: U.S. Department of Health and Human Services

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6426

### 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 antibiotics. 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 antibiotics. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with antibiotics.

#### 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 antibiotics. 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 "antibiotics" (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 "antibiotics". 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 "antibiotics" (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 "antibiotics" (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.[23]

## 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

[23] 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)[24]:

- **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/**

[24] 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 antibiotics:

- **Basic Guidelines for Antibiotics**

  **Antibiotics overdose**
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002675.htm

- **Signs & Symptoms for Antibiotics**

  **Abdominal cramping**
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003120.htm

  **Abdominal pain**
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003120.htm

  **Bluish colored lips and fingernails**
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003215.htm

  **Chest pain**
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003079.htm

**Collapse**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003092.htm

**Convulsions**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003200.htm

**Difficulty breathing**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003075.htm

**Emesis**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

**Fever**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003090.htm

**Nausea and/or vomiting**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003117.htm

**No breathing**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003069.htm

**Pale skin**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003244.htm

**Rash**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003220.htm

**Swelling**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003103.htm

**Wheezing**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003070.htm

- **Background Topics for Antibiotics**

**Breathing problems**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000007.htm

**Respiratory**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002290.htm

**Stop breathing**
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000007.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**

# ANTIBIOTICS DICTIONARY

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

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

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

**Abdominal Pain:** Sensation of discomfort, distress, or agony in the abdominal region. [NIH]

**Abscess:** Accumulation of purulent material in tissues, organs, or circumscribed spaces, usually associated with signs of infection. [NIH]

**Acanthamoeba:** A genus of free-living soil amoebae that produces no flagellate stage. Its organisms are pathogens for several infections in humans and have been found in the eye, bone, brain, and respiratory tract. [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]

**Acetaldehyde:** A colorless, flammable liquid used in the manufacture of acetic acid, perfumes, and flavors. It is also an intermediate in the metabolism of alcohol. It has a general narcotic action and also causes irritation of mucous membranes. Large doses may cause death from respiratory paralysis. [NIH]

**Acetylcholine:** A neurotransmitter. Acetylcholine in vertebrates is the major transmitter at neuromuscular junctions, autonomic ganglia, parasympathetic effector junctions, a subset of sympathetic effector junctions, and at many sites in the central nervous system. It is generally not used as an administered drug because it is broken down very rapidly by cholinesterases, but it is useful in some ophthalmological applications. [NIH]

**Acne:** A disorder of the skin marked by inflammation of oil glands and hair glands. [NIH]

**Acne Vulgaris:** A chronic disorder of the pilosebaceous apparatus associated with an increase in sebum secretion. It is characterized by open comedones (blackheads), closed comedones (whiteheads), and pustular nodules. The cause is unknown, but heredity and age are predisposing factors. [NIH]

**Acremonium:** A mitosporic fungal genus with many reported ascomycetous teleomorphs. Cephalosporin antibiotics are derived from this genus. [NIH]

**Acute renal:** A condition in which the kidneys suddenly stop working. In most cases, kidneys can recover from almost complete loss of function. [NIH]

**Acyclovir:** Functional analog of the nucleoside guanosine. It acts as an antimetabolite, especially in viruses. It is used as an antiviral agent, especially in herpes infections. [NIH]

**Acyl:** Chemical signal used by bacteria to communicate. [NIH]

**Acyl Carrier Protein:** Consists of a polypeptide chain and 4'-phosphopantetheine linked to a serine residue by a phosphodiester bond. Acyl groups are bound as thiol esters to the pantothenyl group. Acyl carrier protein is involved in every step of fatty acid synthesis by the cytoplasmic system. [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]

**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]

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

**Adjuvant:** A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

**Adolescence:** The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

**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]

**Aerobic:** In biochemistry, reactions that need oxygen to happen or happen when oxygen is present. [NIH]

**Aerosol:** A solution of a drug which can be atomized into a fine mist for inhalation therapy. [EU]

**Affinity:** 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

**Affinity Chromatography:** In affinity chromatography, a ligand attached to a column binds specifically to the molecule to be purified. [NIH]

**Agar:** A complex sulfated polymer of galactose units, extracted from Gelidium cartilagineum, Gracilaria confervoides, and related red algae. It is used as a gel in the preparation of solid culture media for microorganisms, as a bulk laxative, in making emulsions, and as a supporting medium for immunodiffusion and immunoelectrophoresis. [NIH]

**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]

**Alanine:** A non-essential amino acid that occurs in high levels in its free state in plasma. It is produced from pyruvate by transamination. It is involved in sugar and acid metabolism, increases immunity, and provides energy for muscle tissue, brain, and the central nervous system. [NIH]

**Aldehyde Dehydrogenase:** An enzyme that oxidizes an aldehyde in the presence of NAD+ and water to an acid and NADH. EC 1.2.1.3. Before 1978, it was classified as EC 1.1.1.70. [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]

**Alkylate:** To treat with an alkylating agent. [EU]

**Alkylation:** The covalent bonding of an alkyl group to an organic compound. It can occur by a simple addition reaction or by substitution of another functional group. [NIH]

**Allantois:** An embryonic diverticulum of the hindgut of reptiles, birds, and mammals; in man its blood vessels give rise to those of the umbilical cord. [NIH]

**Allergen:** An antigenic substance capable of producing immediate-type hypersensitivity (allergy). [EU]

**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]

**Alopecia:** Absence of hair from areas where it is normally present. [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-Defensins:** Defensins found in azurophilic granules of neutrophils and in the secretory granules of intestinal paneth cells. [NIH]

**Alpha-helix:** One of the secondary element of protein. [NIH]

**Alprenolol:** 1-((1-Methylethyl)amino)-3-(2-(2-propenyl)phenoxy)-2-propanol. Adrenergic beta-blocker used as an antihypertensive, anti-anginal, and anti-arrhythmic agent. [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]

**Aluminum:** A metallic element that has the atomic number 13, atomic symbol Al, and atomic weight 26.98. [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]

**Amikacin:** A broad-spectrum antibiotic derived from kanamycin. It is reno- and ototoxic like the other aminoglycoside antibiotics. [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 Motifs:** Commonly observed structural components of proteins formed by simple combinations of adjacent secondary structures. A commonly observed structure may be composed of a conserved sequence which can be represented by a consensus sequence. [NIH]

**Amino Acid Sequence:** The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

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

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

**Aminoethyl:** A protease inhibitor. [NIH]

**Aminopropionitrile:** 3-Aminopropanenitrile. Reagent used as an intermediate in the manufacture of beta-alanine and pantothenic acid. [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]

**Amnion:** The extraembryonic membrane which contains the embryo and amniotic fluid. [NIH]

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

**Amoxicillin:** A broad-spectrum semisynthetic antibiotic similar to ampicillin except that its resistance to gastric acid permits higher serum levels with oral administration. [NIH]

**Ampicillin:** Semi-synthetic derivative of penicillin that functions as an orally active broad-spectrum antibiotic. [NIH]

**Amplification:** The production of additional copies of a chromosomal DNA sequence, found as either intrachromosomal or extrachromosomal DNA. [NIH]

**Anabolic:** Relating to, characterized by, or promoting anabolism. [EU]

**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]

**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]

**Analytes:** A component of a test sample the presence of which has to be demonstrated. The term "analyte" includes where appropriate formed from the analyte during the analyses. [NIH]

**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]

**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]

**Anginal:** Pertaining to or characteristic of angina. [EU]

**Angiogenesis:** Blood vessel formation. Tumor angiogenesis is the growth of blood vessels from surrounding tissue to a solid tumor. This is caused by the release of chemicals by the tumor. [NIH]

**Anhydrides:** Chemical compounds derived from acids by the elimination of a molecule of water. [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]

**Anode:** Electrode held at a positive potential with respect to a cathode. [NIH]

**Anorexia:** Lack or loss of appetite for food. Appetite is psychologic, dependent on memory and associations. Anorexia can be brought about by unattractive food, surroundings, or company. [NIH]

**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]

**Anthracycline:** A member of a family of anticancer drugs that are also antibiotics. [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]

**Antiangiogenic:** Having to do with reducing the growth of new blood vessels. [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]

**Antibiotics, Aminoglycoside:** Antibiotics whose structure contains amino sugars attached to an aminocyclitol ring (hexose nucleus) by glycosidic bonds. Aminoglycoside antibiotics are derived from various species of Streptomyces and Micromonospora or are produced synthetically. They act by inhibiting protein synthesis. [NIH]

**Antibiotics, Combined:** Combinations of antibiotics used against difficult-to-treat infections. Antibiotic combinations have been used mainly to broaden the antibacterial spectrum and prevent development of resistance. In some instances these combinations have shown lower toxicity, but drug antagonism may be one of the problems encountered by their use. They may be given simultaneously or sequentially. The drugs need not be in the same dosage form. [NIH]

**Antibodies:** Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the antigen that induced their synthesis in cells of the lymphoid series (especially plasma cells), or with an antigen closely related to it. [NIH]

**Antibody:** A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. [NIH]

**Anticoagulant:** A drug that helps prevent blood clots from forming. Also called a blood thinner. [NIH]

**Anticodon:** The sequential set of three nucleotides in transfer RNA that interacts with its complement in messenger RNA, the codon, during translation in the ribosome. [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]

**Antifungal:** Destructive to fungi, or suppressing their reproduction or growth; effective against fungal infections. [EU]

**Antifungal Agents:** Substances that destroy fungi by suppressing their ability to grow or reproduce. They differ from fungicides, industrial because they defend against fungi present in human or animal tissues. [NIH]

**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]

**Antigen-presenting cell:** APC. A cell that shows antigen on its surface to other cells of the immune system. This is an important part of an immune response. [NIH]

**Antihypertensive:** An agent that reduces high blood pressure. [EU]

**Anti-infective:** An agent that so acts. [EU]

**Anti-Infective Agents:** Substances that prevent infectious agents or organisms from spreading or kill infectious agents in order to prevent the spread of infection. [NIH]

**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]

**Antioxidant:** A substance that prevents damage caused by free radicals. Free radicals are highly reactive chemicals that often contain oxygen. They are produced when molecules are split to give products that have unpaired electrons. This process is called oxidation. [NIH]

**Antipruritic:** Relieving or preventing itching. [EU]

**Antiseptic:** A substance that inhibits the growth and development of microorganisms without necessarily killing them. [EU]

**Antiviral:** Destroying viruses or suppressing their replication. [EU]

**Antiviral Agents:** Agents used in the prophylaxis or therapy of virus diseases. Some of the ways they may act include preventing viral replication by inhibiting viral DNA polymerase; binding to specific cell-surface receptors and inhibiting viral penetration or uncoating; inhibiting viral protein synthesis; or blocking late stages of virus assembly. [NIH]

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

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

**Anxiolytic:** An anxiolytic or antianxiety agent. [EU]

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

**Aqueous humor:** Clear, watery fluid that flows between and nourishes the lens and the cornea; secreted by the ciliary processes. [NIH]

**Arachidonate 12-Lipoxygenase:** An enzyme that catalyzes the oxidation of arachidonic acid to yield 12-hydroperoxyarachidonate (12-HPETE) which is itself rapidly converted by a peroxidase to 12-hydroxy-5,8,10,14-eicosatetraenoate (12-HETE). The 12-hydroperoxides are preferentially formed in platelets. EC 1.13.11.31. [NIH]

**Arachidonate 15-Lipoxygenase:** An enzyme that catalyzes the oxidation of arachidonic acid to yield 15-hydroperoxyarachidonate (15-HPETE) which is rapidly converted to 15-hydroxy-5,8,11,13-eicosatetraenoate (15-HETE). The 15-hydroperoxides are preferentially formed in neutrophils and lymphocytes. EC 1.13.11.33. [NIH]

**Arachidonate Lipoxygenases:** Enzymes catalyzing the oxidation of arachidonic acid to hydroperoxyarachidonates (HPETES). These products are then rapidly converted by a peroxidase to hydroxyeicosatetraenoic acids (HETES). The positional specificity of the enzyme reaction varies from tissue to tissue. The final lipoxygenase pathway leads to the leukotrienes. EC 1.13.11.- . [NIH]

**Arachidonic Acid:** An unsaturated, essential fatty acid. It is found in animal and human fat as well as in the liver, brain, and glandular organs, and is a constituent of animal phosphatides. It is formed by the synthesis from dietary linoleic acid and is a precursor in the biosynthesis of prostaglandins, thromboxanes, and leukotrienes. [NIH]

**Arginine:** An essential amino acid that is physiologically active in the L-form. [NIH]

**Aromatic:** Having a spicy odour. [EU]

**Arterial:** Pertaining to an artery or to the arteries. [EU]

**Arteries:** The vessels carrying blood away from the heart. [NIH]

**Arterioles:** The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

**Arteriolosclerosis:** Sclerosis and thickening of the walls of the smaller arteries (arterioles). Hyaline arteriolosclerosis, in which there is homogeneous pink hyaline thickening of the arteriolar walls, is associated with benign nephrosclerosis. Hyperplastic arteriolosclerosis, in which there is a concentric thickening with progressive narrowing of the lumina may be associated with malignant hypertension, nephrosclerosis, and scleroderma. [EU]

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

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

**Arteritis:** Inflammation of an artery. [NIH]

**Articular:** Of or pertaining to a joint. [EU]

**Ascorbic Acid:** A six carbon compound related to glucose. It is found naturally in citrus fruits and many vegetables. Ascorbic acid is an essential nutrient in human diets, and necessary to maintain connective tissue and bone. Its biologically active form, vitamin C, functions as a reducing agent and coenzyme in several metabolic pathways. Vitamin C is considered an antioxidant. [NIH]

**Aspartate:** A synthetic amino acid. [NIH]

**Aspartic:** The naturally occurring substance is L-aspartic acid. One of the acidic-amino-acids is obtained by the hydrolysis of proteins. [NIH]

**Aspartic Acid:** One of the non-essential amino acids commonly occurring in the L-form. It is found in animals and plants, especially in sugar cane and sugar beets. It may be a neurotransmitter. [NIH]

**Asphyxia:** A pathological condition caused by lack of oxygen, manifested in impending or actual cessation of life. [NIH]

**Aspiration:** The act of inhaling. [NIH]

**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]

**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]

**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]

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

**Autacoids:** A chemically diverse group of substances produced by various tissues in the body that cause slow contraction of smooth muscle; they have other intense but varied pharmacologic activities. [NIH]

**Authorship:** The profession of writing. Also the identity of the writer as the creator of a literary production. [NIH]

**Autodigestion:** Autolysis; a condition found in disease of the stomach: the stomach wall is digested by the gastric juice. [NIH]

**Autoimmune disease:** A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. [NIH]

**Autolysis:** The spontaneous disintegration of tissues or cells by the action of their own autogenous enzymes. [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]

**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]

**Bactericidal:** Substance lethal to bacteria; substance capable of killing bacteria. [NIH]

**Bacteriocins:** Substances elaborated by specific strains of bacteria that are lethal against other strains of the same or related species. They are protein or lipopolysaccharide-protein complexes used in taxonomy studies of bacteria. [NIH]

**Bacteriolysis:** Rupture of bacterial cells due to mechanical force, chemical action, or the lytic growth of bacteriophages. [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]

**Bacteriophage lambda:** A temperate inducible phage and type species of the genus lambda-like Phages, in the family Siphoviridae. Its natural host is E. coli K12. Its virion contains linear double-stranded DNA, except for 12 complementary bases at the 5'-termini of the polynucleotide chains. The DNA circularizes on infection. [NIH]

**Bacteriostatic:** 1. Inhibiting the growth or multiplication of bacteria. 2. An agent that inhibits the growth or multiplication of bacteria. [EU]

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

**Barbiturate:** A drug with sedative and hypnotic effects. Barbiturates have been used as sedatives and anesthetics, and they have been used to treat the convulsions associated with epilepsy. [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]

**Basophils:** Granular leukocytes characterized by a relatively pale-staining, lobate nucleus and cytoplasm containing coarse dark-staining granules of variable size and stainable by basic dyes. [NIH]

**Benign:** Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

**Benzene:** Toxic, volatile, flammable liquid hydrocarbon biproduct of coal distillation. It is used as an industrial solvent in paints, varnishes, lacquer thinners, gasoline, etc. Benzene causes central nervous system damage acutely and bone marrow damage chronically and is carcinogenic. It was formerly used as parasiticide. [NIH]

**Benzoic Acid:** A fungistatic compound that is widely used as a food preservative. It is conjugated to glycine in the liver and excreted as hippuric acid. [NIH]

**Beta-Defensins:** Defensins found mainly in epithelial cells. [NIH]

**Beta-Lactam Resistance:** Nonsusceptibility of an organism to the action of the beta-lactam antibiotics. [NIH]

**Beta-Lactamases:** Enzymes found in many bacteria which catalyze the hydrolysis of the amide bond in the beta-lactam ring. Well known antibiotics destroyed by these enzymes are penicillins and cephalosporins. EC 3.5.2.6. [NIH]

**Beta-sheet:** Two or more parallel or anti-parallel strands are arranged in rows. [NIH]

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

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

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

**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]

**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]

**Bioassay:** Determination of the relative effective strength of a substance (as a vitamin, hormone, or drug) by comparing its effect on a test organism with that of a standard preparation. [NIH]

**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]

**Biodegradation:** The series of processes by which living organisms degrade pollutant chemicals, organic wastes, pesticides, and implantable materials. [NIH]

**Biofilms:** Films of bacteria or other microbial organisms, usually embedded in extracellular polymers such as implanted medical devices, which adhere to surfaces submerged in, or subjected to, aquatic environments (From Singleton & Sainsbury, Dictionary of Microbiology and Molecular Biology, 2d ed). Biofilms consist of multilayers of microbial cells glued together to form microbial communities which are highly resistant to both phagocytes and antibiotics. [NIH]

**Biological Assay:** A method of measuring the effects of a biologically active substance using an intermediate in vivo or in vitro tissue or cell model under controlled conditions. It includes virulence studies in animal fetuses in utero, mouse convulsion bioassay of insulin, quantitation of tumor-initiator systems in mouse skin, calculation of potentiating effects of a hormonal factor in an isolated strip of contracting stomach muscle, etc. [NIH]

**Biological Factors:** Compounds made by living organisms that contribute to or influence a phenomenon or process. They have biological or physiological activities. [NIH]

**Biological therapy:** Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier (BRM) therapy. [NIH]

**Biological Transport:** The movement of materials (including biochemical substances and drugs) across cell membranes and epithelial layers, usually by passive diffusion. [NIH]

**Biomolecular:** A scientific field at the interface between advanced computing and biotechnology. [NIH]

**Biophysics:** The science of physical phenomena and processes in living organisms. [NIH]

**Biopolymers:** Polymers, such as proteins, DNA, RNA, or polysaccharides formed by any living organism. [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]

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

**Biotransformation:** The chemical alteration of an exogenous substance by or in a biological system. The alteration may inactivate the compound or it may result in the production of an active metabolite of an inactive parent compound. The alteration may be either non-synthetic (oxidation-reduction, hydrolysis) or synthetic (glucuronide formation, sulfate conjugation, acetylation, methylation). This also includes metabolic detoxication and

clearance. [NIH]

**Bladder:** The organ that stores urine. [NIH]

**Bleomycin:** A complex of related glycopeptide antibiotics from Streptomyces verticillus consisting of bleomycin A2 and B2. It inhibits DNA metabolism and is used as an antineoplastic, especially for solid tumors. [NIH]

**Blood Coagulation:** The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [NIH]

**Blood Coagulation Factors:** Endogenous substances, usually proteins, that are involved in the blood coagulation process. [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-Brain Barrier:** Specialized non-fenestrated tightly-joined endothelial cells (tight junctions) that form a transport barrier for certain substances between the cerebral capillaries and the brain tissue. [NIH]

**Body Fluids:** Liquid components of living organisms. [NIH]

**Bone Cements:** Adhesives used to fix prosthetic devices to bones and to cement bone to bone in difficult fractures. Synthetic resins are commonly used as cements. A mixture of monocalcium phosphate, monohydrate, alpha-tricalcium phosphate, and calcium carbonate with a sodium phosphate solution is also a useful bone paste. [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 scan:** A technique to create images of bones on a computer screen or on film. A small amount of radioactive material is injected into a blood vessel and travels through the bloodstream; it collects in the bones and is detected by a scanner. [NIH]

**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]

**Bradykinin:** A nonapeptide messenger that is enzymatically produced from kallidin in the blood where it is a potent but short-lived agent of arteriolar dilation and increased capillary permeability. Bradykinin is also released from mast cells during asthma attacks, from gut walls as a gastrointestinal vasodilator, from damaged tissues as a pain signal, and may be a neurotransmitter. [NIH]

**Brain Ischemia:** Localized reduction of blood flow to brain tissue due to arterial obtruction or systemic hypoperfusion. This frequently occurs in conjuction with brain hypoxia. Prolonged ischemia is associated with brain infarction. [NIH]

**Brain Neoplasms:** Neoplasms of the intracranial components of the central nervous system, including the cerebral hemispheres, basal ganglia, hypothalamus, thalamus, brain stem, and cerebellum. Brain neoplasms are subdivided into primary (originating from brain tissue)

and secondary (i.e., metastatic) forms. Primary neoplasms are subdivided into benign and malignant forms. In general, brain tumors may also be classified by age of onset, histologic type, or presenting location in the brain. [NIH]

**Brain Stem:** The part of the brain that connects the cerebral hemispheres with the spinal cord. It consists of the mesencephalon, pons, and medulla oblongata. [NIH]

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

**Breakdown:** A physical, metal, or nervous collapse. [NIH]

**Broad-spectrum:** Effective against a wide range of microorganisms; said of an antibiotic. [EU]

**Bromine:** A halogen with the atomic symbol Br, atomic number 36, and atomic weight 79.904. It is a volatile reddish-brown liquid that gives off suffocating vapors, is corrosive to the skin, and may cause severe gastroenteritis if ingested. [NIH]

**Bronchi:** The larger air passages of the lungs arising from the terminal bifurcation of the trachea. [NIH]

**Bronchial:** Pertaining to one or more bronchi. [EU]

**Bronchiectasis:** Persistent abnormal dilatation of the bronchi. [NIH]

**Bronchitis:** Inflammation (swelling and reddening) of the bronchi. [NIH]

**Bronchopulmonary:** Pertaining to the lungs and their air passages; both bronchial and pulmonary. [EU]

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

**Buffers:** A chemical system that functions to control the levels of specific ions in solution. When the level of hydrogen ion in solution is controlled the system is called a pH buffer. [NIH]

**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]

**Butadienes:** Four carbon unsaturated hydrocarbons containing two double bonds. [NIH]

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

**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]

**Candidiasis:** Infection with a fungus of the genus Candida. It is usually a superficial infection of the moist cutaneous areas of the body, and is generally caused by C. albicans; it most commonly involves the skin (dermatocandidiasis), oral mucous membranes (thrush, def. 1), respiratory tract (bronchocandidiasis), and vagina (vaginitis). Rarely there is a systemic infection or endocarditis. Called also moniliasis, candidosis, oidiomycosis, and formerly blastodendriosis. [EU]

**Candidosis:** An infection caused by an opportunistic yeasts that tends to proliferate and become pathologic when the environment is favorable and the host resistance is weakened. [NIH]

**Capillary:** Any one of the minute vessels that connect the arterioles and venules, forming a network in nearly all parts of the body. Their walls act as semipermeable membranes for the interchange of various substances, including fluids, between the blood and tissue fluid; called also vas capillare. [EU]

**Capillary Fragility:** The lack of resistance, or susceptibility, of capillaries to damage or disruption under conditions of increased stress. [NIH]

**Capsular:** Cataract which is initiated by an opacification at the surface of the lens. [NIH]

**Capsules:** Hard or soft soluble containers used for the oral administration of medicine. [NIH]

**Captopril:** A potent and specific inhibitor of peptidyl-dipeptidase A. It blocks the conversion of angiotensin I to angiotensin II, a vasoconstrictor and important regulator of arterial blood pressure. Captopril acts to suppress the renin-angiotensin system and inhibits pressure responses to exogenous angiotensin. [NIH]

**Carbapenems:** A group of beta-lactam antibiotics in which the sulfur atom in the thiazolidine ring of the penicillin molecule is replaced by a carbon atom. Thienamycins are a subgroup of carbapenems which have a sulfur atom as the first constituent of the side chain. [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]

**Carboxy:** Cannabinoid. [NIH]

**Carboxylic Acids:** Organic compounds containing the carboxy group (-COOH). This group of compounds includes amino acids and fatty acids. Carboxylic acids can be saturated, unsaturated, or aromatic. [NIH]

**Carboxypeptidases:** Enzymes that act at a free C-terminus of a polypeptide to liberate a single amino acid residue. They are further divided based on their catalytic mechanism into serine-type carboxypeptidases EC 3.4.16; metallocarboxypeptidases, EC 3.4.17; and cysteine-type carboxypeptidases, EC 3.4.18. EC 3.4.-. [NIH]

**Carcinogen:** Any substance that causes cancer. [NIH]

**Carcinogenic:** Producing carcinoma. [EU]

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

**Cardiac arrest:** A sudden stop of heart function. [NIH]

**Cardiotoxicity:** Toxicity that affects the heart. [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]

**Caspases:** A family of intracellular cysteine endopeptidases. They play a key role in inflammation and mammalian apoptosis. They are specific for aspartic acid at the P1 position. They are divided into two classes based on the lengths of their N-terminal prodomains. Caspases-1,-2,-4,-5,-8, and -10 have long prodomains and -3,-6,-7,-9 have short prodomains. EC 3.4.22.-. [NIH]

**Catalytic Domain:** The region of an enzyme that interacts with its substrate to cause the enzymatic reaction. [NIH]

**Catechin:** Extracted from Uncaria gambier, Acacia catechu and other plants; it stabilizes collagen and is therefore used in tanning and dyeing; it prevents capillary fragility and abnormal permeability, but was formerly used as an antidiarrheal. [NIH]

**Catecholamines:** A general class of ortho-dihydroxyphenylalkylamines derived from tyrosine. [NIH]

**Catheters:** A small, flexible tube that may be inserted into various parts of the body to inject or remove liquids. [NIH]

**Cathode:** An electrode, usually an incandescent filament of tungsten, which emits electrons in an X-ray tube. [NIH]

**Cations:** Postively charged atoms, radicals or groups of atoms which travel to the cathode or negative pole during electrolysis. [NIH]

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

**Caustic:** An escharotic or corrosive agent. Called also cauterant. [EU]

**Cauterization:** The destruction of tissue with a hot instrument, an electrical current, or a caustic substance. [NIH]

**Cefazolin:** Semisynthetic cephalosporin analog with broad-spectrum antibiotic action due to inhibition of bacterial cell wall synthesis. It attains high serum levels and is excreted quickly via the urine. [NIH]

**Ceftazidime:** Semisynthetic, broad-spectrum antibacterial derived from cephaloridine and used especially for Pseudomonas and other gram-negative infections in debilitated patients. [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]

**Cefuroxime:** Broad-spectrum cephalosporin antibiotic resistant to beta-lactamase. It has been proposed for infections with gram-negative and gram-positive organisms, gonorrhea, and haemophilus. [NIH]

**Cell:** The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

**Cell Cycle:** The complex series of phenomena, occurring between the end of one cell

division and the end of the next, by which cellular material is divided between daughter cells. [NIH]

**Cell 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 proliferation:** An increase in the number of cells as a result of cell growth and cell division. [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 Survival:** The span of viability of a cell characterized by the capacity to perform certain functions such as metabolism, growth, reproduction, some form of responsiveness, and adaptability. [NIH]

**Cellulitis:** An acute, diffuse, and suppurative inflammation of loose connective tissue, particularly the deep subcutaneous tissues, and sometimes muscle, which is most commonly seen as a result of infection of a wound, ulcer, or other skin lesions. [NIH]

**Cellulose:** A polysaccharide with glucose units linked as in cellobiose. It is the chief constituent of plant fibers, cotton being the purest natural form of the substance. As a raw material, it forms the basis for many derivatives used in chromatography, ion exchange materials, explosives manufacturing, and pharmaceutical preparations. [NIH]

**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]

**Cephaloridine:** A cephalosporin antibiotic. [NIH]

**Cephalosporins:** A group of broad-spectrum antibiotics first isolated from the Mediterranean fungus Acremonium (Cephalosporium acremonium). They contain the beta-lactam moiety thia-azabicyclo-octenecarboxylic acid also called 7-aminocephalosporanic acid. [NIH]

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

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

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

**Cerebral Palsy:** Refers to a motor disability caused by a brain dysfunction. [NIH]

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

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

**Cerebrovascular:** Pertaining to the blood vessels of the cerebrum, or brain. [EU]

**Cerebrovascular Disorders:** A broad category of disorders characterized by impairment of blood flow in the arteries and veins which supply the brain. These include cerebral infarction; brain ischemia; hypoxia, brain; intracranial embolism and thrombosis; intracranial arteriovenous malformations; and vasculitis, central nervous system. In common usage, the term cerebrovascular disorders is not limited to conditions that affect the cerebrum, but refers to vascular disorders of the entire brain including the diencephalon; brain stem; and cerebellum. [NIH]

**Cerebrum:** The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

**Cesarean Section:** Extraction of the fetus by means of abdominal hysterotomy. [NIH]

**Character:** In current usage, approximately equivalent to personality. The sum of the relatively fixed personality traits and habitual modes of response of an individual. [NIH]

**Chemotactic Factors:** Chemical substances that attract or repel cells or organisms. The concept denotes especially those factors released as a result of tissue injury, invasion, or immunologic activity, that attract leukocytes, macrophages, or other cells to the site of infection or insult. [NIH]

**Chemotherapeutics:** Noun plural but singular or plural in constructions : chemotherapy. [EU]

**Chemotherapy:** Treatment with anticancer drugs. [NIH]

**Chest cavity:** Space in body surrounding the lungs. [NIH]

**Chitin Synthase:** An enzyme that converts UDP glucosamine into chitin and UDP. EC 2.4.1.16. [NIH]

**Chlamydia:** A genus of the family Chlamydiaceae whose species cause a variety of diseases in vertebrates including humans, mice, and swine. Chlamydia species are gram-negative and produce glycogen. The type species is Chlamydia trachomatis. [NIH]

**Chlorhexidine:** Disinfectant and topical anti-infective agent used also as mouthwash to prevent oral plaque. [NIH]

**Chlorides:** Inorganic compounds derived from hydrochloric acid that contain the Cl- ion. [NIH]

**Chloroform:** A commonly used laboratory solvent. It was previously used as an anesthetic, but was banned from use in the U.S. due to its suspected carcinogenecity. [NIH]

**Chlorophyll:** Porphyrin derivatives containing magnesium that act to convert light energy in photosynthetic organisms. [NIH]

**Chlortetracycline:** An antibiotic substance isolated from the substrate of Streptomyces aureofaciens and used as an antibacterial and antiprotozoal agent. [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]

**Cholic Acid:** A major primary bile acid produced in the liver and usually conjugated with glycine or taurine. It facilitates fat absorption and cholesterol excretion. [NIH]

**Chorion:** The outermost extraembryonic membrane. [NIH]

**Chorioretinitis:** Inflammation of the choroid in which the sensory retina becomes edematous and opaque. The inflammatory cells and exudate may burst through the sensory retina to cloud the vitreous body. [NIH]

**Choroid:** The thin, highly vascular membrane covering most of the posterior of the eye between the retina and sclera. [NIH]

**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]

**Chromic:** Catgut sterilized and impregnated with chromium trioxide. [NIH]

**Chromium:** A trace element that plays a role in glucose metabolism. It has the atomic symbol Cr, atomic number 24, and atomic weight 52. According to the Fourth Annual Report on Carcinogens (NTP85-002,1985), chromium and some of its compounds have been listed as known carcinogens. [NIH]

**Chromosomal:** Pertaining to chromosomes. [EU]

**Chromosome:** Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

**Chromosome Segregation:** The orderly segregation of chromosomes during meiosis or mitosis. [NIH]

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

**Chronic prostatitis:** Inflammation of the prostate gland, developing slowly and lasting a long time. [NIH]

**Cilastatin:** A renal dehydropeptidase-I and leukotriene D4 dipeptidase inhibitor. Since the antibiotic, imipenem, is hydrolyzed by dehydropeptidase-I, which resides in the brush border of the renal tubule, cilastatin is administered with imipenem to increase its effectiveness. The drug also inhibits the metabolism of leukotriene D4 to leukeotriene E4. [NIH]

**Ciliary:** Inflammation or infection of the glands of the margins of the eyelids. [NIH]

**Ciliary processes:** The extensions or projections of the ciliary body that secrete aqueous humor. [NIH]

**Ciprofloxacin:** A carboxyfluoroquinoline antimicrobial agent that is effective against a wide range of microorganisms. It has been successfully and safely used in the treatment of resistant respiratory, skin, bone, joint, gastrointestinal, urinary, and genital infections. [NIH]

**Circulatory system:** The system that contains the heart and the blood vessels and moves blood throughout the body. This system helps tissues get enough oxygen and nutrients, and it helps them get rid of waste products. The lymph system, which connects with the blood system, is often considered part of the circulatory system. [NIH]

**Circumcision:** Excision of the prepuce or part of it. [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]

**Citrus:** Any tree or shrub of the Rue family or the fruit of these plants. [NIH]

**Clamp:** A u-shaped steel rod used with a pin or wire for skeletal traction in the treatment of certain fractures. [NIH]

**Clarithromycin:** A semisynthetic macrolide antibiotic derived from erythromycin that is active against a variety of microorganisms. It can inhibit protein synthesis in bacteria by reversibly binding to the 50S ribosomal subunits. This inhibits the translocation of aminoacyl transfer-RNA and prevents peptide chain elongation. [NIH]

**Clavulanic Acid:** Clavulanic acid (C8H9O5N) and its salts and esters. The acid is a suicide inhibitor of bacterial beta-lactamase enzymes from Streptomyces clavuligerus. Administered alone, it has only weak antibacterial activity against most organisms, but given in combination with beta-lactam antibiotics prevents antibiotic inactivation by microbial lactamase. [NIH]

**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 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]

**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]

**Coal:** A natural fuel formed by partial decomposition of vegetable matter under certain environmental conditions. [NIH]

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

**Cod Liver Oil:** Oil obtained from fresh livers of the cod family, Gadidae. It is a source of vitamins A and D. [NIH]

**Codon:** A set of three nucleotides in a protein coding sequence that specifies individual amino acids or a termination signal (codon, terminator). Most codons are universal, but some organisms do not produce the transfer RNAs (RNA, transfer) complementary to all codons. These codons are referred to as unassigned codons (codons, nonsense). [NIH]

**Coenzyme:** An organic nonprotein molecule, frequently a phosphorylated derivative of a water-soluble vitamin, that binds with the protein molecule (apoenzyme) to form the active enzyme (holoenzyme). [EU]

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

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

**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]

**Coliphages:** Viruses whose host is Escherichia coli. [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]

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

**Colony-Stimulating Factors:** Glycoproteins found in a subfraction of normal mammalian plasma and urine. They stimulate the proliferation of bone marrow cells in agar cultures and the formation of colonies of granulocytes and/or macrophages. The factors include interleukin-3 (IL-3), granulocyte colony-stimulating factor (G-CSF), macrophage colony-stimulating factor (M-CSF), and granulocyte-macrophage colony-stimulating factor (GM-CSF). [NIH]

**Combination chemotherapy:** Treatment using more than one anticancer drug. [NIH]

**Combinatorial:** A cut-and-paste process that churns out thousands of potentially valuable compounds at once. [NIH]

**Complement:** A term originally used to refer to the heat-labile factor in serum that causes immune cytolysis, the lysis of antibody-coated cells, and now referring to the entire functionally related system comprising at least 20 distinct serum proteins that is the effector not only of immune cytolysis but also of other biologic functions. Complement activation occurs by two different sequences, the classic and alternative pathways. The proteins of the classic pathway are termed 'components of complement' and are designated by the symbols C1 through C9. C1 is a calcium-dependent complex of three distinct proteins C1q, C1r and C1s. The proteins of the alternative pathway (collectively referred to as the properdin system) and complement regulatory proteins are known by semisystematic or trivial names. Fragments resulting from proteolytic cleavage of complement proteins are designated with lower-case letter suffixes, e.g., C3a. Inactivated fragments may be designated with the suffix 'i', e.g. C3bi. Activated components or complexes with biological activity are designated by a bar over the symbol e.g. C1 or C4b,2a. The classic pathway is activated by the binding of C1 to classic pathway activators, primarily antigen-antibody complexes containing IgM, IgG1, IgG3; C1q binds to a single IgM molecule or two adjacent IgG molecules. The alternative pathway can be activated by IgA immune complexes and also by nonimmunologic materials including bacterial endotoxins, microbial polysaccharides, and cell walls. Activation of the classic pathway triggers an enzymatic cascade involving C1, C4, C2 and C3; activation of the alternative pathway triggers a cascade involving C3 and factors B, D and P. Both result in the cleavage of C5 and the formation of the membrane attack complex. Complement activation also results in the formation of many biologically active complement fragments that act as anaphylatoxins, opsonins, or chemotactic factors. [EU]

**Complementary and alternative medicine:** CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

**Complementary medicine:** Practices not generally recognized by the medical community as standard or conventional medical approaches and used to enhance or complement the standard treatments. Complementary medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

**Complete remission:** The disappearance of all signs of cancer. Also called a complete response. [NIH]

**Compress:** A plug used to occludate an orifice in the control of bleeding, or to mop up secretions; an absorbent pad. [NIH]

**Computational Biology:** A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

**Computed tomography:** CT scan. A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized tomography and computerized axial tomography (CAT) scan. [NIH]

**Computer Simulation:** Computer-based representation of physical systems and phenomena such as chemical processes. [NIH]

**Computerized axial tomography:** A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called CAT scan, computed tomography (CT scan), or computerized tomography. [NIH]

**Conception:** The onset of pregnancy, marked by implantation of the blastocyst; the formation of a viable zygote. [EU]

**Concomitant:** Accompanying; accessory; joined with another. [EU]

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

**Conjugated:** Acting or operating as if joined; simultaneous. [EU]

**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]

**Conjunctiva:** The mucous membrane that lines the inner surface of the eyelids and the anterior part of the sclera. [NIH]

**Connective Tissue:** Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

**Connective Tissue:** Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

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

**Connective Tissue Diseases:** A heterogeneous group of disorders, some hereditary, others acquired, characterized by abnormal structure or function of one or more of the elements of connective tissue, i.e., collagen, elastin, or the mucopolysaccharides. [NIH]

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

**Consensus Sequence:** A theoretical representative nucleotide or amino acid sequence in which each nucleotide or amino acid is the one which occurs most frequently at that site in the different sequences which occur in nature. The phrase also refers to an actual sequence which approximates the theoretical consensus. A known conserved sequence set is represented by a consensus sequence. Commonly observed supersecondary protein structures (amino acid motifs) are often formed by conserved sequences. [NIH]

**Conserved Sequence:** A sequence of amino acids in a polypeptide or of nucleotides in DNA or RNA that is similar across multiple species. A known set of conserved sequences is represented by a consensus sequence. Amino acid motifs are often composed of conserved sequences. [NIH]

**Constitutional:** 1. Affecting the whole constitution of the body; not local. 2. Pertaining to the constitution. [EU]

**Constriction:** The act of constricting. [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]

**Contraceptive:** An agent that diminishes the likelihood of or prevents conception. [EU]

**Contractility:** Capacity for becoming short in response to a suitable stimulus. [EU]

**Contraindications:** Any factor or sign that it is unwise to pursue a certain kind of action or treatment, e. g. giving a general anesthetic to a person with pneumonia. [NIH]

**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]

**Convulsion:** A violent involuntary contraction or series of contractions of the voluntary muscles. [EU]

**Coordination:** Muscular or motor regulation or the harmonious cooperation of muscles or groups of muscles, in a complex action or series of actions. [NIH]

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

**Corneal Transplantation:** Partial or total replacement of the cornea from one human or

animal to another. [NIH]

**Corneal Ulcer:** Loss of epithelial tissue from the surface of the cornea due to progressive erosion and necrosis of the tissue; usually caused by bacterial, fungal, or viral infection. [NIH]

**Coronary:** Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

**Coronary heart disease:** A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

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

**Corpus:** The body of the uterus. [NIH]

**Corpuscle:** A small mass or body; a sensory nerve end bulb; a cell, especially that of the blood or the lymph. [NIH]

**Corrosion:** Irreversible destruction of skin tissue. [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]

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

**Cost-benefit:** A quantitative technique of economic analysis which, when applied to radiation practice, compares the health detriment from the radiation doses concerned with the cost of radiation dose reduction in that practice. [NIH]

**Coumarin:** A fluorescent dye. [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]

**Culture Media:** Any liquid or solid preparation made specifically for the growth, storage, or transport of microorganisms or other types of cells. The variety of media that exist allow for the culturing of specific microorganisms and cell types, such as differential media, selective media, test media, and defined media. Solid media consist of liquid media that have been solidified with an agent such as agar or gelatin. [NIH]

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

**Curettage:** Removal of tissue with a curette, a spoon-shaped instrument with a sharp edge. [NIH]

**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]

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

**Cyclooxygenase Inhibitors:** Compounds or agents that combine with cyclooxygenase

(prostaglandin-endoperoxide synthase) and thereby prevent its substrate-enzyme combination with arachidonic acid and the formation of eicosanoids, prostaglandins, and thromboxanes. [NIH]

**Cyclophosphamide:** Precursor of an alkylating nitrogen mustard antineoplastic and immunosuppressive agent that must be activated in the liver to form the active aldophosphamide. It is used in the treatment of lymphomas, leukemias, etc. Its side effect, alopecia, has been made use of in defleecing sheep. Cyclophosphamide may also cause sterility, birth defects, mutations, and cancer. [NIH]

**Cystamine:** A radiation-protective agent that interferes with sulfhydryl enzymes. It may also protect against carbon tetrachloride liver damage. [NIH]

**Cysteamine:** A radiation-protective agent that oxidizes in air to form cystamine. It can be given intravenously or orally to treat radiation sickness. The bitartrate has been used for the oral treatment of nephropathic cystinosis. [NIH]

**Cysteine:** A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

**Cysteine Endopeptidases:** Endopeptidases which have a cysteine involved in the catalytic process. This group of enzymes is inactivated by sulfhydryl reagents. EC 3.4.22. [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]

**Cytochrome b:** Cytochromes (electron-transporting proteins) with protoheme or a related heme as the prosthetic group. The prosthetic group is not covalently bound to the protein moiety. [NIH]

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

**Cytoplasm:** The protoplasm of a cell exclusive of that of the nucleus; it consists of a continuous aqueous solution (cytosol) and the organelles and inclusions suspended in it (phaneroplasm), and is the site of most of the chemical activities of the cell. [EU]

**Cytotoxic:** Cell-killing. [NIH]

**Cytotoxicity:** Quality of being capable of producing a specific toxic action upon cells of special organs. [NIH]

**Dairy Products:** Raw and processed or manufactured milk and milk-derived products. These are usually from cows (bovine) but are also from goats, sheep, reindeer, and water buffalo. [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]

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

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

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

**Defensins:** Family of antimicrobial peptides that have been identified in humans, animals, and plants. They are thought to play a role in host defenses against infections, inflammation, wound repair, and acquired immunity. Based on the disulfide pairing of their characteristic six cysteine residues, they are divided into alpha-defensins and beta-defensins. [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]

**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]

**Dendrites:** Extensions of the nerve cell body. They are short and branched and receive stimuli from other neurons. [NIH]

**Dendritic:** 1. Branched like a tree. 2. Pertaining to or possessing dendrites. [EU]

**Dendritic cell:** A special type of antigen-presenting cell (APC) that activates T lymphocytes. [NIH]

**Density:** The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

**Dental Caries:** Localized destruction of the tooth surface initiated by decalcification of the enamel followed by enzymatic lysis of organic structures and leading to cavity formation. If left unchecked, the cavity may penetrate the enamel and dentin and reach the pulp. The three most prominent theories used to explain the etiology of the disase are that acids produced by bacteria lead to decalcification; that micro-organisms destroy the enamel protein; or that keratolytic micro-organisms produce chelates that lead to decalcification. [NIH]

**Dental implant:** A small metal pin placed inside the jawbone to mimic the root of a tooth. Dental implants can be used to help anchor a false tooth or teeth, or a crown or bridge. [NIH]

**Dental Plaque:** A film that attaches to teeth, often causing dental caries and gingivitis. It is

composed of mucins, secreted from salivary glands, and microorganisms. [NIH]

**Dentists:** Individuals licensed to practice dentistry. [NIH]

**Deoxyribonucleic:** A polymer of subunits called deoxyribonucleotides which is the primary genetic material of a cell, the material equivalent to genetic information. [NIH]

**Deoxyribonucleic acid:** A polymer of subunits called deoxyribonucleotides which is the primary genetic material of a cell, the material equivalent to genetic information. [NIH]

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

**Depressive Disorder:** An affective disorder manifested by either a dysphoric mood or loss of interest or pleasure in usual activities. The mood disturbance is prominent and relatively persistent. [NIH]

**Depsipeptide:** Anticancer drugs obtained from microorganisms. [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]

**Detergents:** Purifying or cleansing agents, usually salts of long-chain aliphatic bases or acids, that exert cleansing (oil-dissolving) and antimicrobial effects through a surface action that depends on possessing both hydrophilic and hydrophobic properties. [NIH]

**Detoxification:** Treatment designed to free an addict from his drug habit. [EU]

**Deuterium:** Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [NIH]

**Developed Countries:** Countries that have reached a level of economic achievement through an increase of production, per capita income and consumption, and utilization of natural and human resources. [NIH]

**Dexamethasone:** (11 beta,16 alpha)-9-Fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione. An anti-inflammatory glucocorticoid used either in the free alcohol or esterified form in treatment of conditions that respond generally to cortisone. [NIH]

**Diabetes Mellitus:** A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

**Diabetic Retinopathy:** Retinopathy associated with diabetes mellitus, which may be of the background type, progressively characterized by microaneurysms, interretinal punctuate macular edema, or of the proliferative type, characterized by neovascularization of the retina and optic disk, which may project into the vitreous, proliferation of fibrous tissue, vitreous hemorrhage, and retinal detachment. [NIH]

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

**Dialyzer:** A part of the hemodialysis machine. (See hemodialysis under dialysis.) The dialyzer has two sections separated by a membrane. One section holds dialysate. The other holds the patient's blood. [NIH]

**Diarrhea:** Passage of excessively liquid or excessively frequent stools. [NIH]

**Diarrhoea:** Abnormal frequency and liquidity of faecal discharges. [EU]

**Diencephalon:** The paired caudal parts of the prosencephalon from which the thalamus, hypothalamus, epithalamus, and subthalamus are derived. [NIH]

**Diffusion:** The tendency of a gas or solute to pass from a point of higher pressure or

concentration to a point of lower pressure or concentration and to distribute itself throughout the available space; a major mechanism of biological transport. [NIH]

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

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

**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]

**Digital rectal examination:** DRE. An examination in which a doctor inserts a lubricated, gloved finger into the rectum to feel for abnormalities. [NIH]

**Dihydroxy:** AMPA/Kainate antagonist. [NIH]

**Dilatation:** The act of dilating. [NIH]

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

**Diploid:** Having two sets of chromosomes. [NIH]

**Direct:** 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

**Disease Vectors:** Invertebrates or non-human vertebrates which transmit infective organisms from one host to another. [NIH]

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

**Disinfection:** Rendering pathogens harmless through the use of heat, antiseptics, antibacterial agents, etc. [NIH]

**Dissociation:** 1. The act of separating or state of being separated. 2. The separation of a molecule into two or more fragments (atoms, molecules, ions, or free radicals) produced by the absorption of light or thermal energy or by solvation. 3. In psychology, a defense mechanism in which a group of mental processes are segregated from the rest of a person's mental activity in order to avoid emotional distress, as in the dissociative disorders (q.v.), or in which an idea or object is segregated from its emotional significance; in the first sense it is roughly equivalent to splitting, in the second, to isolation. 4. A defect of mental integration in which one or more groups of mental processes become separated off from normal consciousness and, thus separated, function as a unitary whole. [EU]

**Distal:** Remote; farther from any point of reference; opposed to proximal. In dentistry, used to designate a position on the dental arch farther from the median line of the jaw. [EU]

**Disulfiram:** A carbamate derivative used as an alcohol deterrent. It is a relatively nontoxic substance when administered alone, but markedly alters the intermediary metabolism of alcohol. When alcohol is ingested after administration of disulfiram, blood acetaldehyde concentrations are increased, followed by flushing, systemic vasodilation, respiratory difficulties, nausea, hypotension, and other symptoms (acetaldehyde syndrome). It acts by inhibiting aldehyde dehydrogenase. [NIH]

**Diuresis:** Increased excretion of urine. [EU]

**Docetaxel:** An anticancer drug that belongs to the family of drugs called mitotic inhibitors. [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]

**Dosage Forms:** Completed forms of the pharmaceutical preparation in which prescribed doses of medication are included. They are designed to resist action by gastric fluids, prevent vomiting and nausea, reduce or alleviate the undesirable taste and smells associated with oral administration, achieve a high concentration of drug at target site, or produce a delayed or long-acting drug effect. They include capsules, liniments, ointments, pharmaceutical solutions, powders, tablets, etc. [NIH]

**Doxorubicin:** Antineoplastic antibiotic obtained from Streptomyces peucetics. It is a hydroxy derivative of daunorubicin and is used in treatment of both leukemia and solid tumors. [NIH]

**Doxycycline:** A synthetic tetracycline derivative with a range of antimicrobial activity and mode of action similar to that of tetracycline, but more effective against many species. Animal studies suggest that it may cause less tooth staining than other tetracyclines. [NIH]

**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 Delivery Systems:** Systems of administering drugs through controlled delivery so that an optimum amount reaches the target site. Drug delivery systems encompass the carrier, route, and target. [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 Resistance:** Diminished or failed response of an organism, disease or tissue to the intended effectiveness of a chemical or drug. It should be differentiated from drug tolerance which is the progressive diminution of the susceptibility of a human or animal to the effects of a drug, as a result of continued administration. [NIH]

**Drug Tolerance:** Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

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

**Duodenum:** The first part of the small intestine. [NIH]

**Dura mater:** The outermost, toughest, and most fibrous of the three membranes (meninges) covering the brain and spinal cord; called also pachymeninx. [EU]

**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]

**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]

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

**Effector:** It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

**Effector cell:** A cell that performs a specific function in response to a stimulus; usually used to describe cells in the immune system. [NIH]

**Efficacy:** The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomized control trial. [NIH]

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

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

**Ejaculation:** The release of semen through the penis during orgasm. [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]

**Emboli:** Bit of foreign matter which enters the blood stream at one point and is carried until it is lodged or impacted in an artery and obstructs it. It may be a blood clot, an air bubble, fat or other tissue, or clumps of bacteria. [NIH]

**Embolism:** Blocking of a blood vessel by a blood clot or foreign matter that has been transported from a distant site by the blood stream. [NIH]

**Embolization:** The blocking of an artery by a clot or foreign material. Embolization can be done as treatment to block the flow of blood to a tumor. [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]

**Emepronium:** A muscarinic antagonist used mainly in the treatment of urinary syndromes. It is incompletely absorbed from the gastrointestinal tract and does not cross the blood-brain barrier. [NIH]

**Emesis:** Vomiting; an act of vomiting. Also used as a word termination, as in haematemesis. [EU]

**Empiric:** Empirical; depending upon experience or observation alone, without using scientific method or theory. [EU]

**Empyema:** Presence of pus in a hollow organ or body cavity. [NIH]

**Emulsion:** A preparation of one liquid distributed in small globules throughout the body of a second liquid. The dispersed liquid is the discontinuous phase, and the dispersion medium is the continuous phase. When oil is the dispersed liquid and an aqueous solution is the continuous phase, it is known as an oil-in-water emulsion, whereas when water or aqueous solution is the dispersed phase and oil or oleaginous substance is the continuous phase, it is known as a water-in-oil emulsion. Pharmaceutical emulsions for which official standards have been promulgated include cod liver oil emulsion, cod liver oil emulsion with malt, liquid petrolatum emulsion, and phenolphthalein in liquid petrolatum emulsion. [EU]

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

**Encapsulated:** Confined to a specific, localized area and surrounded by a thin layer of tissue. [NIH]

**Endocarditis:** Exudative and proliferative inflammatory alterations of the endocardium, characterized by the presence of vegetations on the surface of the endocardium or in the endocardium itself, and most commonly involving a heart valve, but sometimes affecting the inner lining of the cardiac chambers or the endocardium elsewhere. It may occur as a primary disorder or as a complication of or in association with another disease. [EU]

**Endocardium:** The innermost layer of the heart, comprised of endothelial cells. [NIH]

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

**Endocrinology:** A subspecialty of internal medicine concerned with the metabolism, physiology, and disorders of the endocrine system. [NIH]

**Endometrium:** The layer of tissue that lines the uterus. [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]

**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, Lymphatic:** Unbroken cellular lining (intima) of the lymph vessels (e.g., the high endothelial lymphatic venules). It is more permeable than vascular endothelium, lacking selective absorption and functioning mainly to remove plasma proteins that have filtered through the capillaries into the tissue spaces. [NIH]

**Endothelium, Vascular:** Single pavement layer of cells which line the luminal surface of the entire vascular system and regulate the transport of macromolecules and blood components from interstitium to lumen; this function has been most intensively studied in the blood capillaries. [NIH]

**Endothelium-derived:** Small molecule that diffuses to the adjacent muscle layer and relaxes it. [NIH]

**Endotoxin:** Toxin from cell walls of bacteria. [NIH]

**Enhancer:** Transcriptional element in the virus genome. [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]

**Enterocolitis:** Inflammation of the intestinal mucosa of the small and large bowel. [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]

**Enzyme Inhibitors:** Compounds or agents that combine with an enzyme in such a manner as to prevent the normal substrate-enzyme combination and the catalytic reaction. [NIH]

**Eosinophils:** Granular leukocytes with a nucleus that usually has two lobes connected by a slender thread of chromatin, and cytoplasm containing coarse, round granules that are uniform in size and stainable by eosin. [NIH]

**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]

**Epigastric:** Having to do with the upper middle area of the abdomen. [NIH]

**Epirubicin:** An anthracycline antibiotic which is the 4'-epi-isomer of doxorubicin. The compound exerts its antitumor effects by interference with the synthesis and function of DNA. Clinical studies indicate activity in breast cancer, non-Hodgkin's lymphomas, ovarian cancer, soft-tissue sarcomas, pancreatic cancer, gastric cancer, small-cell lung cancer and acute leukemia. It is equal in activity to doxorubicin but exhibits less acute toxicities and less cardiotoxicity. [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]

**Erectile:** The inability to get or maintain an erection for satisfactory sexual intercourse. Also called impotence. [NIH]

**Erythrocyte Membrane:** The semipermeable outer portion of the red corpuscle. It is known as a 'ghost' after hemolysis. [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]

**Estradiol:** The most potent mammalian estrogenic hormone. It is produced in the ovary, placenta, testis, and possibly the adrenal cortex. [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]

**Ethnic Groups:** A group of people with a common cultural heritage that sets them apart from others in a variety of social relationships. [NIH]

**Etoposide:** A semisynthetic derivative of podophyllotoxin that exhibits antitumor activity. Etoposide inhibits DNA synthesis by forming a complex with topoisomerase II and DNA. This complex induces breaks in double stranded DNA and prevents repair by topoisomerase II binding. Accumulated breaks in DNA prevent entry into the mitotic phase of cell division, and lead to cell death. Etoposide acts primarily in the G2 and S phases of the cell cycle. [NIH]

**Eukaryotic Cells:** Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

**Evacuation:** An emptying, as of the bowels. [EU]

**Excipients:** Usually inert substances added to a prescription in order to provide suitable consistency to the dosage form; a binder, matrix, base or diluent in pills, tablets, creams, salves, etc. [NIH]

**Excitability:** Property of a cardiac cell whereby, when the cell is depolarized to a critical level (called threshold), the membrane becomes permeable and a regenerative inward current causes an action potential. [NIH]

**Excitation:** An act of irritation or stimulation or of responding to a stimulus; the addition of energy, as the excitation of a molecule by absorption of photons. [EU]

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

**Excitatory Amino Acids:** Endogenous amino acids released by neurons as excitatory neurotransmitters. Glutamic acid is the most common excitatory neurotransmitter in the brain. Aspartic acid has been regarded as an excitatory transmitter for many years, but the extent of its role as a transmitter is unclear. [NIH]

**Exocrine:** Secreting outwardly, via a duct. [EU]

**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]

**Expectorant:** 1. Promoting the ejection, by spitting, of mucus or other fluids from the lungs and trachea. 2. An agent that promotes the ejection of mucus or exudate from the lungs, bronchi, and trachea; sometimes extended to all remedies that quiet cough (antitussives). [EU]

**Extender:** Any of several colloidal substances of high molecular weight, used as a blood or plasma substitute in transfusion for increasing the volume of the circulating blood. [NIH]

**Extracellular:** Outside a cell or cells. [EU]

**Extracellular Matrix:** A meshwork-like substance found within the extracellular space and in association with the basement membrane of the cell surface. It promotes cellular proliferation and provides a supporting structure to which cells or cell lysates in culture dishes adhere. [NIH]

**Extracellular Matrix Proteins:** Macromolecular organic compounds that contain carbon, hydrogen, oxygen, nitrogen, and usually, sulfur. These macromolecules (proteins) form an intricate meshwork in which cells are embedded to construct tissues. Variations in the relative types of macromolecules and their organization determine the type of extracellular matrix, each adapted to the functional requirements of the tissue. The two main classes of macromolecules that form the extracellular matrix are: glycosaminoglycans, usually linked to proteins (proteoglycans), and fibrous proteins (e.g., collagen, elastin, fibronectins and laminin). [NIH]

**Extracellular Space:** Interstitial space between cells, occupied by fluid as well as amorphous and fibrous substances. [NIH]

**Extraction:** The process or act of pulling or drawing out. [EU]

**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]

**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]

**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]

**Fermentation:** An enzyme-induced chemical change in organic compounds that takes place

in the absence of oxygen. The change usually results in the production of ethanol or lactic acid, and the production of energy. [NIH]

**Fertilizers:** Substances or mixtures that are added to the soil to supply nutrients or to make available nutrients already present in the soil, in order to increase plant growth and productivity. [NIH]

**Fetal Blood:** Blood of the fetus. Exchange of nutrients and waste between the fetal and maternal blood occurs via the placenta. The cord blood is blood contained in the umbilical vessels at the time of delivery. [NIH]

**Fetal Membranes:** Thin layers of tissue which surround the embryo or fetus and provide for its nutrition, respiration, excretion and protection; they are the yolk sac, allantois, amnion, and chorion. [NIH]

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

**Fibrin:** A protein derived from fibrinogen in the presence of thrombin, which forms part of the blood clot. [NIH]

**Fibrinogen:** Plasma glycoprotein clotted by thrombin, composed of a dimer of three non-identical pairs of polypeptide chains (alpha, beta, gamma) held together by disulfide bonds. Fibrinogen clotting is a sol-gel change involving complex molecular arrangements: whereas fibrinogen is cleaved by thrombin to form polypeptides A and B, the proteolytic action of other enzymes yields different fibrinogen degradation products. [NIH]

**Fibrosis:** Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

**Fistulas:** An abnormal passage from one hollow structure of the body to another, or from a hollow structure to the surface, formed by an abscess, disease process, incomplete closure of a wound, or by a congenital anomaly. [NIH]

**Flatus:** Gas passed through the rectum. [NIH]

**Flavoring Agents:** Substances added to foods and medicine to improve the quality of taste. [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]

**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]

**Flushing:** A transient reddening of the face that may be due to fever, certain drugs, exertion, stress, or a disease process. [NIH]

**Fold:** A plication or doubling of various parts of the body. [NIH]

**Food Handling:** Any aspect of the operations in the preparation, transport, storage, packaging, wrapping, exposure for sale, service, or delivery of food. [NIH]

**Foramen:** A natural hole of perforation, especially one in a bone. [NIH]

**Forearm:** The part between the elbow and the wrist. [NIH]

**Fosfomycin:** An antibiotic produced by Streptomyces fradiae. [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]

**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]

**Fungicides, Industrial:** Chemicals that kill or inhibit the growth of fungi in agricultural applications, on wood, plastics, or other materials, in swimming pools, etc. [NIH]

**Fungistatic:** Inhibiting the growth of fungi. [EU]

**Fungus:** A general term used to denote a group of eukaryotic protists, including mushrooms, yeasts, rusts, moulds, smuts, etc., which are characterized by the absence of chlorophyll and by the presence of a rigid cell wall composed of chitin, mannans, and sometimes cellulose. They are usually of simple morphological form or show some reversible cellular specialization, such as the formation of pseudoparenchymatous tissue in the fruiting body of a mushroom. The dimorphic fungi grow, according to environmental conditions, as moulds or yeasts. [EU]

**Gallate:** Antioxidant present in tea. [NIH]

**Gallbladder:** The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

**Ganglia:** Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

**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]

**Gasoline:** Volative flammable fuel (liquid hydrocarbons) derived from crude petroleum by processes such as distillation reforming, polymerization, etc. [NIH]

**Gastric:** Having to do with the stomach. [NIH]

**Gastric Acid:** Hydrochloric acid present in gastric juice. [NIH]

**Gastritis:** Inflammation of the stomach. [EU]

**Gastroenteritis:** An acute inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhoea, abdominal pain, and weakness, which has various causes, including food poisoning due to infection with such organisms as Escherichia coli, Staphylococcus aureus, and Salmonella species; consumption of irritating food or drink; or psychological factors such as anger, stress, and fear. Called also enterogastritis. [EU]

**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]

**Gastrointestinal:** Refers to the stomach and intestines. [NIH]

**Gastrointestinal tract:** The stomach and intestines. [NIH]

**Gelatin:** A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [NIH]

**Gene:** The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein. [NIH]

**Gene Expression:** The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

**Generator:** Any system incorporating a fixed parent radionuclide from which is produced a daughter radionuclide which is to be removed by elution or by any other method and used in a radiopharmaceutical. [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]

**Genetics:** The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

**Genital:** Pertaining to the genitalia. [EU]

**Genotype:** The genetic constitution of the individual; the characterization of the genes. [NIH]

**Germ Cells:** The reproductive cells in multicellular organisms. [NIH]

**Gestation:** The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

**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]

**Glomeruli:** Plural of glomerulus. [NIH]

**Glucocorticoid:** A compound that belongs to the family of compounds called corticosteroids (steroids). Glucocorticoids affect metabolism and have anti-inflammatory and immunosuppressive effects. They may be naturally produced (hormones) or synthetic (drugs). [NIH]

**Glucose:** D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

**Glutamate:** Excitatory neurotransmitter of the brain. [NIH]

**Glutamic Acid:** A non-essential amino acid naturally occurring in the L-form. Glutamic acid (glutamate) is the most common excitatory neurotransmitter in the central nervous system. [NIH]

**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]

**Glutathione Peroxidase:** An enzyme catalyzing the oxidation of 2 moles of glutathione in the presence of hydrogen peroxide to yield oxidized glutathione and water. EC 1.11.1.9. [NIH]

**Glycerol:** A trihydroxy sugar alcohol that is an intermediate in carbohydrate and lipid metabolism. It is used as a solvent, emollient, pharmaceutical agent, and sweetening agent. [NIH]

**Glycerophospholipids:** Derivatives of phosphatidic acid in which the hydrophobic regions are composed of two fatty acids and a polar alcohol is joined to the C-3 position of glycerol through a phosphodiester bond. They are named according to their polar head groups, such as phosphatidylcholine and phosphatidylethanolamine. [NIH]

**Glycine:** A non-essential amino acid. It is found primarily in gelatin and silk fibroin and used therapeutically as a nutrient. It is also a fast inhibitory neurotransmitter. [NIH]

**Glycogen:** A sugar stored in the liver and muscles. It releases glucose into the blood when cells need it for energy. Glycogen is the chief source of stored fuel in the body. [NIH]

**Glycopeptides:** Proteins which contain carbohydrate groups attached covalently to the polypeptide chain. The protein moiety is the predominant group with the carbohydrate making up only a small percentage of the total weight. [NIH]

**Glycoprotein:** A protein that has sugar molecules attached to it. [NIH]

**Glycoside:** Any compound that contains a carbohydrate molecule (sugar), particularly any such natural product in plants, convertible, by hydrolytic cleavage, into sugar and a nonsugar component (aglycone), and named specifically for the sugar contained, as glucoside (glucose), pentoside (pentose), fructoside (fructose) etc. [EU]

**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]

**Gonadal:** Pertaining to a gonad. [EU]

**Gonorrhea:** Acute infectious disease characterized by primary invasion of the urogenital tract. The etiologic agent, Neisseria gonorrhoeae, was isolated by Neisser in 1879. [NIH]

**Governing Board:** The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

**Government Agencies:** Administrative units of government responsible for policy making and management of governmental activities in the U.S. and abroad. [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]

**Grafting:** The operation of transfer of tissue from one site to another. [NIH]

**Gram-negative:** Losing the stain or decolorized by alcohol in Gram's method of staining, a primary characteristic of bacteria having a cell wall composed of a thin layer of peptidoglycan covered by an outer membrane of lipoprotein and lipopolysaccharide. [EU]

**Gram-Negative Bacteria:** Bacteria which lose crystal violet stain but are stained pink when treated by Gram's method. [NIH]

**Gram-positive:** Retaining the stain or resisting decolorization by alcohol in Gram's method of staining, a primary characteristic of bacteria whose cell wall is composed of a thick layer of peptidologlycan with attached teichoic acids. [EU]

**Gram-Positive Bacteria:** Bacteria which retain the crystal violet stain when treated by Gram's method. [NIH]

**Granule:** A small pill made from sucrose. [EU]

**Granulocyte Colony-Stimulating Factor:** A glycoprotein of MW 25 kDa containing internal disulfide bonds. It induces the survival, proliferation, and differentiation of neutrophilic granulocyte precursor cells and functionally activates mature blood neutrophils. Among the family of colony-stimulating factors, G-CSF is the most potent inducer of terminal differentiation to granulocytes and macrophages of leukemic myeloid cell lines. [NIH]

**Granulocytes:** Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

**Granulomatous Disease, Chronic:** A recessive X-linked defect of leukocyte function in which phagocytic cells ingest but fail to digest bacteria, resulting in recurring bacterial infections with granuloma formation. [NIH]

**Grasses:** A large family, Gramineae, of narrow-leaved herbaceous monocots. Many grasses produce highly allergenic pollens and are hosts to cattle parasites and toxic fungi. [NIH]

**Growth:** The progressive development of a living being or part of an organism from its earliest stage to maturity. [NIH]

**Growth factors:** Substances made by the body that function to regulate cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy. [NIH]

**Guanidine:** A strong organic base existing primarily as guanidium ions at physiological pH. It is found in the urine as a normal product of protein metabolism. It is also used in laboratory research as a protein denaturant. (From Martindale, the Extra Pharmacopoeia, 30th ed and Merck Index, 12th ed) It is also used in the treatment of myasthenia and as a fluorescent probe in HPLC. [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]

**Gynecology:** A medical-surgical specialty concerned with the physiology and disorders primarily of the female genital tract, as well as female endocrinology and reproductive physiology. [NIH]

**Gyrase:** An enzyme that causes negative supercoiling of E. coli DNA during replication. [NIH]

**Habitual:** Of the nature of a habit; according to habit; established by or repeated by force of habit, customary. [EU]

**Haematemesis:** The vomiting of blood. [EU]

**Haemophilus:** A genus of Pasteurellaceae that consists of several species occurring in animals and humans. Its organisms are described as gram-negative, facultatively anaerobic, coccobacillus or rod-shaped, and nonmotile. [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]

**Halitosis:** An offensive, foul breath odor resulting from a variety of causes such as poor oral hygiene, dental or oral infections, or the ingestion of certain foods. [NIH]

**Haploid:** An organism with one basic chromosome set, symbolized by n; the normal condition of gametes in diploids. [NIH]

**Haptens:** Small antigenic determinants capable of eliciting an immune response only when coupled to a carrier. Haptens bind to antibodies but by themselves cannot elicit an antibody response. [NIH]

**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 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]

**Heart Valves:** Flaps of tissue that prevent regurgitation of blood from the ventricles to the atria or from the pulmonary arteries or aorta to the ventricles. [NIH]

**Heartburn:** Substernal pain or burning sensation, usually associated with regurgitation of gastric juice into the esophagus. [NIH]

**Hematoma:** An extravasation of blood localized in an organ, space, or tissue. [NIH]

**Heme:** The color-furnishing portion of hemoglobin. It is found free in tissues and as the prosthetic group in many hemeproteins. [NIH]

**Hemodiafiltration:** The combination of hemodialysis and hemofiltration either simultaneously or sequentially. Convective transport (hemofiltration) may be better for removal of larger molecular weight substances and diffusive transport (hemodialysis) for smaller molecular weight solutes. [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]

**Hemofiltration:** Extracorporeal ultrafiltration technique without hemodialysis for treatment of fluid overload and electrolyte disturbances affecting renal, cardiac, or pulmonary function. [NIH]

**Hemolysis:** The destruction of erythrocytes by many different causal agents such as antibodies, bacteria, chemicals, temperature, and changes in tonicity. [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]

**Hemopneumothorax:** Collection of air and blood in the pleural cavity. [NIH]

**Hemorrhage:** Bleeding or escape of blood from a vessel. [NIH]

**Hemorrhagic stroke:** A disorder involving bleeding within ischemic brain tissue. Hemorrhagic stroke occurs when blood vessels that are damaged or dead from lack of blood supply (infarcted), located within an area of infarcted brain tissue, rupture and transform an "ischemic" stroke into a hemorrhagic stroke. Ischemia is inadequate tissue oxygenation caused by reduced blood flow; infarction is tissue death resulting from ischemia. Bleeding irritates the brain tissues, causing swelling (cerebral edema). Blood collects into a mass (hematoma). Both swelling and hematoma will compress and displace brain tissue. [NIH]

**Hemothorax:** Hemorrhage within the pleural cavity. [NIH]

**Herbicides:** Pesticides used to destroy unwanted vegetation, especially various types of weeds, grasses, and woody plants. [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 virus:** A member of the herpes family of viruses. [NIH]

**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]

**Heterotrophic:** Pertaining to organisms that are consumers and dependent on other organisms for their source of energy (food). [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]

**Homogeneous:** Consisting of or composed of similar elements or ingredients; of a uniform quality throughout. [EU]

**Homologous:** Corresponding in structure, position, origin, etc., as (a) the feathers of a bird and the scales of a fish, (b) antigen and its specific antibody, (c) allelic chromosomes. [EU]

**Hormonal:** Pertaining to or of the nature of a hormone. [EU]

**Hormone:** A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

**Host:** Any animal that receives a transplanted graft. [NIH]

**Hybrid:** Cross fertilization between two varieties or, more usually, two species of vines, see

also crossing. [NIH]

**Hybridization:** The genetic process of crossbreeding to produce a hybrid. Hybrid nucleic acids can be formed by nucleic acid hybridization of DNA and RNA molecules. Protein hybridization allows for hybrid proteins to be formed from polypeptide chains. [NIH]

**Hydration:** Combining with water. [NIH]

**Hydrocephalus:** Excessive accumulation of cerebrospinal fluid within the cranium which may be associated with dilation of cerebral ventricles, intracranial hypertension; headache; lethargy; urinary incontinence; and ataxia (and in infants macrocephaly). This condition may be caused by obstruction of cerebrospinal fluid pathways due to neurologic abnormalities, intracranial hemorrhages; central nervous system infections; brain neoplasms; craniocerebral trauma; and other conditions. Impaired resorption of cerebrospinal fluid from the arachnoid villi results in a communicating form of hydrocephalus. Hydrocephalus ex-vacuo refers to ventricular dilation that occurs as a result of brain substance loss from cerebral infarction and other conditions. [NIH]

**Hydrochloric Acid:** A strong corrosive acid that is commonly used as a laboratory reagent. It is formed by dissolving hydrogen chloride in water. Gastric acid is the hydrochloric acid component of gastric juice. [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]

**Hydrolases:** Any member of the class of enzymes that catalyze the cleavage of the substrate and the addition of water to the resulting molecules, e.g., esterases, glycosidases (glycoside hydrolases), lipases, nucleotidases, peptidases (peptide hydrolases), and phosphatases (phosphoric monoester hydrolases). EC 3. [NIH]

**Hydrolysis:** The process of cleaving a chemical compound by the addition of a molecule of water. [NIH]

**Hydrophilic:** Readily absorbing moisture; hygroscopic; having strongly polar groups that readily interact with water. [EU]

**Hydrophobic:** Not readily absorbing water, or being adversely affected by water, as a hydrophobic colloid. [EU]

**Hydroxylation:** Hydroxylate, to introduce hydroxyl into (a compound or radical) usually by replacement of hydrogen. [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]

**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]

**Hypnotic:** A drug that acts to induce sleep. [EU]

**Hypodermic:** Applied or administered beneath the skin. [EU]

**Hypoglycemia:** Abnormally low blood sugar [NIH]

**Hypotension:** Abnormally low blood pressure. [NIH]

**Hypoxia:** Reduction of oxygen supply to tissue below physiological levels despite adequate perfusion of the tissue by blood. [EU]

**Hysterotomy:** An incision in the uterus, performed through either the abdomen or the vagina. [NIH]

**Id:** The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

**Imidazole:** C3H4N2. The ring is present in polybenzimidazoles. [NIH]

**Imipenem:** Semisynthetic thienamycin that has a wide spectrum of antibacterial activity against gram-negative and gram-positive aerobic and anaerobic bacteria, including many multiresistant strains. It is stable to beta-lactamases. Clinical studies have demonstrated high efficacy in the treatment of infections of various body systems. Its effectiveness is enhanced when it is administered in combination with cilastatin, a renal dipeptidase inhibitor. [NIH]

**Immune adjuvant:** A drug that stimulates the immune system to respond to disease. [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 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]

**Immunocompromised:** Having a weakened immune system caused by certain diseases or treatments. [NIH]

**Immunodeficiency:** The decreased ability of the body to fight infection and disease. [NIH]

**Immunoglobulin:** A protein that acts as an antibody. [NIH]

**Immunohistochemistry:** Histochemical localization of immunoreactive substances using labeled antibodies as reagents. [NIH]

**Immunologic:** The ability of the antibody-forming system to recall a previous experience with an antigen and to respond to a second exposure with the prompt production of large amounts of antibody. [NIH]

**Immunology:** The study of the body's immune system. [NIH]

**Immunosuppressive:** Describes the ability to lower immune system responses. [NIH]

**Immunosuppressive Agents:** Agents that suppress immune function by one of several mechanisms of action. Classical cytotoxic immunosuppressants act by inhibiting DNA synthesis. Others may act through activation of suppressor T-cell populations or by inhibiting the activation of helper cells. While immunosuppression has been brought about in the past primarily to prevent rejection of transplanted organs, new applications involving mediation of the effects of interleukins and other cytokines are emerging. [NIH]

**Impairment:** In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

**Implantation:** The insertion or grafting into the body of biological, living, inert, or

radioactive material. [EU]

**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]

**Incontinence:** Inability to control the flow of urine from the bladder (urinary incontinence) or the escape of stool from the rectum (fecal incontinence). [NIH]

**Incubated:** Grown in the laboratory under controlled conditions. (For instance, white blood cells can be grown in special conditions so that they attack specific cancer cells when returned to the body.) [NIH]

**Indicative:** That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

**Indomethacin:** A non-steroidal anti-inflammatory agent (NSAID) that inhibits the enzyme cyclooxygenase necessary for the formation of prostaglandins and other autacoids. It also inhibits the motility of polymorphonuclear leukocytes. [NIH]

**Induction:** The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

**Infarction:** A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

**Infection:** 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local infection may persist and spread by extension to become an acute, subacute, or chronic clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

**Infection Control:** Programs of disease surveillance, generally within health care facilities, designed to investigate, prevent, and control the spread of infections and their causative microorganisms. [NIH]

**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]

**Infuse:** To pour (a liquid) into something. [EU]

**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]

**Initiator:** A chemically reactive substance which may cause cell changes if ingested, inhaled or absorbed into the body; the substance may thus initiate a carcinogenic process. [NIH]

**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]

**Insecticides:** Pesticides designed to control insects that are harmful to man. The insects may be directly harmful, as those acting as disease vectors, or indirectly harmful, as destroyers of crops, food products, or textile fabrics. [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]

**Instillation:** . [EU]

**Insulator:** Material covering the metal conductor of the lead. It is usually polyurethane or silicone. [NIH]

**Insulin:** A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

**Integrase:** An enzyme that inserts DNA into the host genome. It is encoded by the pol gene of retroviruses and also by temperate bacteriophages, the best known being bacteriophage lambda. EC 2.7.7.-. [NIH]

**Intensive Care:** Advanced and highly specialized care provided to medical or surgical patients whose conditions are life-threatening and require comprehensive care and constant monitoring. It is usually administered in specially equipped units of a health care facility. [NIH]

**Interferons:** Proteins secreted by vertebrate cells in response to a wide variety of inducers. They confer resistance against many different viruses, inhibit proliferation of normal and malignant cells, impede multiplication of intracellular parasites, enhance macrophage and granulocyte phagocytosis, augment natural killer cell activity, and show several other immunomodulatory functions. [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-10:** Factor that is a coregulator of mast cell growth. It is produced by T-cells and B-cells and shows extensive homology with the Epstein-Barr virus BCRFI gene. [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]

**Interleukins:** Soluble factors which stimulate growth-related activities of leukocytes as well as other cell types. They enhance cell proliferation and differentiation, DNA synthesis, secretion of other biologically active molecules and responses to immune and inflammatory stimuli. [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]

**Interstitial:** Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

**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 Embolism:** The sudden obstruction of a blood vessel by an embolus. [NIH]

**Intracranial Embolism and Thrombosis:** Embolism or thrombosis involving blood vessels which supply intracranial structures. Emboli may originate from extracranial or intracranial sources. Thrombosis may occur in arterial or venous structures. [NIH]

**Intracranial Hemorrhages:** Bleeding within the intracranial cavity, including hemorrhages in the brain and within the cranial epidural, subdural, and subarachnoid spaces. [NIH]

**Intracranial Hypertension:** Increased pressure within the cranial vault. This may result from several conditions, including hydrocephalus; brain edema; intracranial masses; severe systemic hypertension; pseudotumor cerebri; and other disorders. [NIH]

**Intracranial Pressure:** Pressure within the cranial cavity. It is influenced by brain mass, the circulatory system, CSF dynamics, and skull rigidity. [NIH]

**Intramuscular:** IM. Within or into muscle. [NIH]

**Intraocular:** Within the eye. [EU]

**Intravenous:** IV. Into a vein. [NIH]

**Intrinsic:** Situated entirely within or pertaining exclusively to a part. [EU]

**Invasive:** 1. Having the quality of invasiveness. 2. Involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

**Invertebrates:** Animals that have no spinal column. [NIH]

**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 Exchange:** Reversible chemical reaction between a solid, often an ION exchange resin, and a fluid whereby ions may be exchanged from one substance to another. This technique is used in water purification, in research, and in industry. [NIH]

**Ionizing:** Radiation comprising charged particles, e. g. electrons, protons, alpha-particles, etc., having sufficient kinetic energy to produce ionization by collision. [NIH]

**Ions:** An atom or group of atoms that have a positive or negative electric charge due to a gain (negative charge) or loss (positive charge) of one or more electrons. Atoms with a positive charge are known as cations; those with a negative charge are anions. [NIH]

**Iris:** The most anterior portion of the uveal layer, separating the anterior chamber from the

posterior. It consists of two layers - the stroma and the pigmented epithelium. Color of the iris depends on the amount of melanin in the stroma on reflection from the pigmented epithelium. [NIH]

**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]

**Isotretinoin:** A topical dermatologic agent that is used in the treatment of acne vulgaris and several other skin diseases. The drug has teratogenic and other adverse effects. [NIH]

**Joint:** The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

**Kanamycin:** Antibiotic complex produced by Streptomyces kanamyceticus from Japanese soil. Comprises 3 components: kanamycin A, the major component, and kanamycins B and C, the minor components. [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]

**Keratin:** A class of fibrous proteins or scleroproteins important both as structural proteins and as keys to the study of protein conformation. The family represents the principal constituent of epidermis, hair, nails, horny tissues, and the organic matrix of tooth enamel. Two major conformational groups have been characterized, alpha-keratin, whose peptide backbone forms an alpha-helix, and beta-keratin, whose backbone forms a zigzag or pleated sheet structure. [NIH]

**Keratitis:** Inflammation of the cornea. [NIH]

**Keratolytic:** An agent that promotes keratolysis. [EU]

**Keto:** It consists of 8 carbon atoms and within the endotoxins, it connects poysaccharide and lipid A. [NIH]

**Killer Cells:** Lymphocyte-like effector cells which mediate antibody-dependent cell cytotoxicity. They kill antibody-coated target cells which they bind with their Fc receptors. [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]

**Labyrinth:** The internal ear; the essential part of the organ of hearing. It consists of an osseous and a membranous portion. [NIH]

**Lacrimal:** Pertaining to the tears. [EU]

**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]

**Lactobacillus acidophilus:** A species of gram-positive, rod-shaped bacteria isolated from the intestinal tract of humans and animals, the human mouth, and vagina. This organism produces the fermented product, acidophilus milk. [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]

**Larynx:** An irregularly shaped, musculocartilaginous tubular structure, lined with mucous membrane, located at the top of the trachea and below the root of the tongue and the hyoid bone. It is the essential sphincter guarding the entrance into the trachea and functioning secondarily as the organ of voice. [NIH]

**Latent:** Phoria which occurs at one distance or another and which usually has no troublesome effect. [NIH]

**Lathyrism:** A paralytic condition of the legs caused by ingestion of lathyrogens, especially beta-aminopropionitrile, found in the seeds of plants of the genus Lathyrus. [NIH]

**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]

**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]

**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]

**Life cycle:** The successive stages through which an organism passes from fertilized ovum or spore to the fertilized ovum or spore of the next generation. [NIH]

**Life Expectancy:** A figure representing the number of years, based on known statistics, to which any person of a given age may reasonably expect to live. [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]

**Ligation:** Application of a ligature to tie a vessel or strangulate a part. [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]

**Lipid:** Fat. [NIH]

**Lipid Bilayers:** Layers of lipid molecules which are two molecules thick. Bilayer systems are frequently studied as models of biological membranes. [NIH]

**Lipid Peroxidation:** Peroxidase catalyzed oxidation of lipids using hydrogen peroxide as an electron acceptor. [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]

**Liposomal:** A drug preparation that contains the active drug in very tiny fat particles. This fat-encapsulated drug is absorbed better, and its distribution to the tumor site is improved. [NIH]

**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]

**Lipoxygenase Inhibitors:** Compounds or agents that combine with lipoxygenase and thereby prevent its substrate-enzyme combination with arachidonic acid and the formation of the eicosanoid products hydroxyeicosatetraenoic acid and various leukotrienes. [NIH]

**Lithium:** An element in the alkali metals family. It has the atomic symbol Li, atomic number 3, and atomic weight 6.94. Salts of lithium are used in treating manic-depressive disorders. [NIH]

**Liver:** A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

**Liver scan:** An image of the liver created on a computer screen or on film. A radioactive substance is injected into a blood vessel and travels through the bloodstream. It collects in the liver, especially in abnormal areas, and can be detected by the scanner. [NIH]

**Lobe:** A portion of an organ such as the liver, lung, breast, or brain. [NIH]

**Localization:** The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

**Localized:** Cancer which has not metastasized yet. [NIH]

**Locomotion:** Movement or the ability to move from one place or another. It can refer to humans, vertebrate or invertebrate animals, and microorganisms. [NIH]

**Longitudinal study:** Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

**Long-Term Care:** Care over an extended period, usually for a chronic condition or disability, requiring periodic, intermittent, or continuous care. [NIH]

**Loop:** A wire usually of platinum bent at one end into a small loop (usually 4 mm inside diameter) and used in transferring microorganisms. [NIH]

**Lubricants:** Oily or slippery substances. [NIH]

**Lymph:** The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

**Lymphatic:** The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

**Lymphatic system:** The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

**Lymphocyte:** A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases. [NIH]

**Lymphoid:** Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

**Lysine:** An essential amino acid. It is often added to animal feed. [NIH]

**Lysostaphin:** A 25 kD peptidase produced by Staphylococcus simulans which cleaves a glycine-glcyine bond unique to an inter-peptide cross-bridge of the Staphylococcus aureus cell wall. EC 3.4.24.75. [NIH]

**Lytic:** 1. Pertaining to lysis or to a lysin. 2. Producing lysis. [EU]

**Macrolides:** A group of organic compounds that contain a macrocyclic lactone ring linked glycosidically to one or more sugar moieties. [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]

**Magnetic Resonance Imaging:** Non-invasive method of demonstrating internal anatomy based on the principle that atomic nuclei in a strong magnetic field absorb pulses of radiofrequency energy and emit them as radiowaves which can be reconstructed into computerized images. The concept includes proton spin tomographic techniques. [NIH]

**Maintenance therapy:** Treatment that is given to help a primary (original) treatment keep working. Maintenance therapy is often given to help keep cancer in remission. [NIH]

**Malaise:** A vague feeling of bodily discomfort. [EU]

**Malignant:** Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

**Malignant tumor:** A tumor capable of metastasizing. [NIH]

**Mammary:** Pertaining to the mamma, or breast. [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]

**Man-made:** Ionizing radiation emitted by artificial or concentrated natural, radioactive material or resulting from the operation of high voltage apparatus, such as X-ray apparatus or particle accelerators, of nuclear reactors, or from nuclear explosions. [NIH]

**Mannans:** Polysaccharides consisting of mannose units. [NIH]

**Mastitis:** Inflammatory disease of the breast, or mammary gland. [NIH]

**Mastoiditis:** Inflammation of the cavity and air cells in the mastoid part of the temporal bone. [NIH]

**Matrix metalloproteinase:** A member of a group of enzymes that can break down proteins, such as collagen, that are normally found in the spaces between cells in tissues (i.e., extracellular matrix proteins). Because these enzymes need zinc or calcium atoms to work properly, they are called metalloproteinases. Matrix metalloproteinases are involved in wound healing, angiogenesis, and tumor cell metastasis. [NIH]

**Maxillary:** Pertaining to the maxilla : the irregularly shaped bone that with its fellow forms the upper jaw. [EU]

**Maxillary Sinus:** One of the paired paranasal sinuses, located in the body of the maxilla, communicating with the middle meatus of the nasal cavity. [NIH]

**Maxillary Sinusitis:** Inflammation of the maxillary sinus. In most cases it is the result of infection by the bacteria Haemophilus influenzae, Streptococcus pneumoniae, and Staphylococcus aureus. This condition may be acute or chronic. [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]

**Meatus:** A canal running from the internal auditory foramen through the petrous portion of the temporal bone. It gives passage to the facial and auditory nerves together with the auditory branch of the basilar artery and the internal auditory veins. [NIH]

**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]

**MEDLINE:** An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

**Megacolon:** Pathological enlargement of the colon. [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]

**Membrane:** A very thin layer of tissue that covers a surface. [NIH]

**Membrane Fusion:** The adherence of cell membranes, intracellular membranes, or artifical membrane models of either to each other or to viruses, parasites, or interstitial particles through a variety of chemical and physical processes. [NIH]

**Membrane Potentials:** Ratio of inside versus outside concentration of potassium, sodium, chloride and other ions in diffusible tissues or cells. Also called transmembrane and resting potentials, they are measured by recording electrophysiologic responses in voltage-dependent ionic channels of (e.g.) nerve, muscle and blood cells as well as artificial membranes. [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]

**Meningitis:** Inflammation of the meninges. When it affects the dura mater, the disease is termed pachymeningitis; when the arachnoid and pia mater are involved, it is called leptomeningitis, or meningitis proper. [EU]

**Meniscus:** A fibro-cartilage within a joint, especially of the knee. [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]

**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]

**Mesenteric:** Pertaining to the mesentery : a membranous fold attaching various organs to the body wall. [EU]

**Mesentery:** A layer of the peritoneum which attaches the abdominal viscera to the abdominal wall and conveys their blood vessels and nerves. [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]

**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]

**Methionine:** A sulfur containing essential amino acid that is important in many body functions. It is a chelating agent for heavy metals. [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]

**Microdialysis:** A technique for measuring extracellular concentrations of substances in tissues, usually in vivo, by means of a small probe equipped with a semipermeable membrane. Substances may also be introduced into the extracellular space through the membrane. [NIH]

**Microorganism:** An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

**Micro-organism:** An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

**Microscopy:** The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

**Migration:** The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

**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]

**Minocycline:** A semisynthetic antibiotic effective against tetracycline-resistant staphylococcus infections. [NIH]

**Miscible:** Susceptible of being mixed. [EU]

**Mitochondria:** Parts of a cell where aerobic production (also known as cell respiration) takes place. [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]

**Mitomycin:** An antineoplastic antibiotic produced by Streptomyces caespitosus. It acts as a bi- or trifunctional alkylating agent causing cross-linking of DNA and inhibition of DNA synthesis. [NIH]

**Mitosis:** A method of indirect cell division by means of which the two daughter nuclei normally receive identical complements of the number of chromosomes of the somatic cells of the species. [NIH]

**Mitotic:** Cell resulting from mitosis. [NIH]

**Mitotic inhibitors:** Drugs that kill cancer cells by interfering with cell division (mitostis). [NIH]

**Mobility:** Capability of movement, of being moved, or of flowing freely. [EU]

**Mobilization:** The process of making a fixed part or stored substance mobile, as by separating a part from surrounding structures to make it accessible for an operative procedure or by causing release into the circulation for body use of a substance stored in the body. [EU]

**Modeling:** A treatment procedure whereby the therapist presents the target behavior which the learner is to imitate and make part of his repertoire. [NIH]

**Modification:** A change in an organism, or in a process in an organism, that is acquired from its own activity or environment. [NIH]

**Molecular:** Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

**Molecular Structure:** The location of the atoms, groups or ions relative to one another in a

molecule, as well as the number, type and location of covalent bonds. [NIH]

**Molecule:** A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

**Monitor:** An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

**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]

**Monobactams:** Monocyclic, bacterially produced or semisynthetic beta-lactam antibiotics. They lack the double ring construction of the traditional beta-lactam antibiotics and can be easily synthesized. [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]

**Morphological:** Relating to the configuration or the structure of live organs. [NIH]

**Motility:** The ability to move spontaneously. [EU]

**Motion Sickness:** Sickness caused by motion, as sea sickness, train sickness, car sickness, and air sickness. [NIH]

**Motor Activity:** The physical activity of an organism as a behavioral phenomenon. [NIH]

**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]

**Multicenter study:** A clinical trial that is carried out at more than one medical institution. [NIH]

**Multiple Myeloma:** A malignant tumor of plasma cells usually arising in the bone marrow; characterized by diffuse involvement of the skeletal system, hyperglobulinemia, Bence-Jones proteinuria, and anemia. [NIH]

**Multiple sclerosis:** A disorder of the central nervous system marked by weakness, numbness, a loss of muscle coordination, and problems with vision, speech, and bladder control. Multiple sclerosis is thought to be an autoimmune disease in which the body's immune system destroys myelin. Myelin is a substance that contains both protein and fat (lipid) and serves as a nerve insulator and helps in the transmission of nerve signals. [NIH]

**Mustard Gas:** Severe irritant and vesicant of skin, eyes, and lungs. It may cause blindness and lethal lung edema and was formerly used as a war gas. The substance has been proposed as a cytostatic and for treatment of psoriasis. It has been listed as a known carcinogen in the Fourth Annual Report on Carcinogens (NTP-85-002, 1985) (Merck, 11th ed). [NIH]

**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]

**Myasthenia:** Muscular debility; any constitutional anomaly of muscle. [EU]

**Mycoplasma:** A genus of gram-negative, facultatively anaerobic bacteria bounded by a plasma membrane only. Its organisms are parasites and pathogens, found on the mucous membranes of humans, animals, and birds. [NIH]

**Myelin:** The fatty substance that covers and protects nerves. [NIH]

**Myeloma:** Cancer that arises in plasma cells, a type of white blood cell. [NIH]

**Myocardial infarction:** Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

**Myocardium:** The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

**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]

**Naloxone:** A specific opiate antagonist that has no agonist activity. It is a competitive antagonist at mu, delta, and kappa opioid receptors. [NIH]

**Naltrexone:** Derivative of noroxymorphone that is the N-cyclopropylmethyl congener of naloxone. It is a narcotic antagonist that is effective orally, longer lasting and more potent than naloxone, and has been proposed for the treatment of heroin addiction. The FDA has approved naltrexone for the treatment of alcohol dependence. [NIH]

**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]

**Natural killer cells:** NK cells. A type of white blood cell that contains granules with enzymes that can kill tumor cells or microbial cells. Also called large granular lymphocytes (LGL). [NIH]

**Natural selection:** A part of the evolutionary process resulting in the survival and reproduction of the best adapted individuals. [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]

**Nebramycin:** A complex of antibiotic substances produced by Streptomyces tenebrarius. [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]

**Neomycin:** Antibiotic complex produced by Streptomyces fradiae. It is composed of neomycins A, B, and C. It acts by inhibiting translation during protein synthesis. [NIH]

**Neonatal:** Pertaining to the first four weeks after birth. [EU]

**Nerve:** A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

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

**Neural:** 1. Pertaining to a nerve or to the nerves. 2. Situated in the region of the spinal axis, as the neutral arch. [EU]

**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]

**Neurogenic:** Loss of bladder control caused by damage to the nerves controlling the bladder. [NIH]

**Neurologic:** Having to do with nerves or the nervous system. [NIH]

**Neuromuscular:** Pertaining to muscles and nerves. [EU]

**Neuronal:** Pertaining to a neuron or neurons (= conducting cells of the nervous system). [EU]

**Neurons:** The basic cellular units of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system. [NIH]

**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]

**Neuropeptides:** Peptides released by neurons as intercellular messengers. Many neuropeptides are also hormones released by non-neuronal cells. [NIH]

**Neuroprotective Agents:** Drugs intended to prevent damage to the brain or spinal cord from ischemia, stroke, convulsions, or trauma. Some must be administered before the event, but others may be effective for some time after. They act by a variety of mechanisms, but often directly or indirectly minimize the damage produced by endogenous excitatory amino acids. [NIH]

**Neuroretinitis:** Inflammation of the optic nerve head and adjacent retina. [NIH]

**Neurotransmitters:** Endogenous signaling molecules that alter the behavior of neurons or effector cells. Neurotransmitter is used here in its most general sense, including not only messengers that act directly to regulate ion channels, but also those that act through second messenger systems, and those that act at a distance from their site of release. Included are neuromodulators, neuroregulators, neuromediators, and neurohumors, whether or not acting at synapses. [NIH]

**Neutrons:** Electrically neutral elementary particles found in all atomic nuclei except light hydrogen; the mass is equal to that of the proton and electron combined and they are unstable when isolated from the nucleus, undergoing beta decay. Slow, thermal, epithermal, and fast neutrons refer to the energy levels with which the neutrons are ejected from heavier nuclei during their decay. [NIH]

**Neutropenia:** An abnormal decrease in the number of neutrophils, a type of white blood cell. [NIH]

**Neutrophils:** Granular leukocytes having a nucleus with three to five lobes connected by slender threads of chromatin, and cytoplasm containing fine inconspicuous granules and stainable by neutral dyes. [NIH]

**Niacin:** Water-soluble vitamin of the B complex occurring in various animal and plant tissues. Required by the body for the formation of coenzymes NAD and NADP. Has pellagra-curative, vasodilating, and antilipemic properties. [NIH]

**Nisin:** A 34-amino acid polypeptide antibiotic produced by Streptococcus lactis. It has been used as a food preservative in canned fruits and vegetables, and cheese. [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]

**Noel:** The highest dose level of a chemical that, in a given toxicity test, causes no observable adverse effect in the test animals. [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]

**Novobiocin:** An antibiotic drug used to treat infection. [NIH]

**Nuclear:** A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

**Nuclei:** A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

**Nucleic acid:** Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

**Nucleic Acid Hybridization:** The process whereby two single-stranded polynucleotides form a double-stranded molecule, with hydrogen bonding between the complementary bases in the two strains. [NIH]

**Nucleolus:** 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]

**Nucleoprotein:** Chromosomes consist largely of nuclei acids and proteins, joined here as complexes called nucleoproteins. [NIH]

**Nucleotidases:** A class of enzymes that catalyze the conversion of a nucleotide and water to a nucleoside and orthophosphate. EC 3.1.3.-. [NIH]

**Nucleus:** A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

**Obstetrics:** A medical-surgical specialty concerned with management and care of women during pregnancy, parturition, and the puerperium. [NIH]

**Ocular:** 1. Of, pertaining to, or affecting the eye. 2. Eyepiece. [EU]

**Odds Ratio:** The ratio of two odds. The exposure-odds ratio for case control data is the ratio of the odds in favor of exposure among cases to the odds in favor of exposure among noncases. The disease-odds ratio for a cohort or cross section is the ratio of the odds in favor of disease among the exposed to the odds in favor of disease among the unexposed. The prevalence-odds ratio refers to an odds ratio derived cross-sectionally from studies of prevalent cases. [NIH]

**Odour:** A volatile emanation that is perceived by the sense of smell. [EU]

**Ofloxacin:** An orally administered broad-spectrum quinolone antibacterial drug active against most gram-negative and gram-positive bacteria. [NIH]

**Ointments:** Semisolid preparations used topically for protective emollient effects or as a vehicle for local administration of medications. Ointment bases are various mixtures of fats, waxes, animal and plant oils and solid and liquid hydrocarbons. [NIH]

**Oligoribonucleotides:** A group of ribonucleotides (up to 12) in which the phosphate residues of each ribonucleotide act as bridges in forming diester linkages between the ribose moieties. [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]

**Oncology:** The study of cancer. [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]

**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]

**Ophthalmic:** Pertaining to the eye. [EU]

**Opportunistic Infections:** An infection caused by an organism which becomes pathogenic under certain conditions, e.g., during immunosuppression. [NIH]

**Optic Disk:** The portion of the optic nerve seen in the fundus with the ophthalmoscope. It is formed by the meeting of all the retinal ganglion cell axons as they enter the optic nerve.

[NIH]

**Optic Nerve:** The 2nd cranial nerve. The optic nerve conveys visual information from the retina to the brain. The nerve carries the axons of the retinal ganglion cells which sort at the optic chiasm and continue via the optic tracts to the brain. The largest projection is to the lateral geniculate nuclei; other important targets include the superior colliculi and the suprachiasmatic nuclei. Though known as the second cranial nerve, it is considered part of the central nervous system. [NIH]

**Oral Health:** The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [NIH]

**Oral Hygiene:** The practice of personal hygiene of the mouth. It includes the maintenance of oral cleanliness, tissue tone, and general preservation of oral health. [NIH]

**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]

**Organ Transplantation:** Transference of an organ between individuals of the same species or between individuals of different species. [NIH]

**Organelles:** Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum; lysomomes; plastids; and vacuoles. [NIH]

**Orofacial:** Of or relating to the mouth and face. [EU]

**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]

**Osteomyelitis:** Inflammation of bone caused by a pyogenic organism. It may remain localized or may spread through the bone to involve the marrow, cortex, cancellous tissue, and periosteum. [EU]

**Otitis:** Inflammation of the ear, which may be marked by pain, fever, abnormalities of hearing, hearing loss, tinnitus, and vertigo. [EU]

**Otitis Media:** Inflammation of the middle ear. [NIH]

**Otitis Media with Effusion:** Inflammation of the middle ear with a clear pale yellow-colored transudate. [NIH]

**Ototoxic:** Having a deleterious effect upon the eighth nerve, or upon the organs of hearing and balance. [EU]

**Outpatient:** A patient who is not an inmate of a hospital but receives diagnosis or treatment in a clinic or dispensary connected with the hospital. [NIH]

**Ovary:** Either of the paired glands in the female that produce the female germ cells and secrete some of the female sex hormones. [NIH]

**Overdose:** An accidental or deliberate dose of a medication or street drug that is in excess of what is normally used. [NIH]

**Ovum:** A female germ cell extruded from the ovary at ovulation. [NIH]

**Ownership:** The legal relation between an entity (individual, group, corporation, or-profit,

secular, government) and an object. The object may be corporeal, such as equipment, or completely a creature of law, such as a patent; it may be movable, such as an animal, or immovable, such as a building. [NIH]

**Oxazolidinones:** Derivatives of oxazolidin-2-one. They represent an important class of synthetic antibiotic agents. [NIH]

**Oxidants:** Oxidizing agents or electron-accepting molecules in chemical reactions in which electrons are transferred from one molecule to another (oxidation-reduction). In vivo, it appears that phagocyte-generated oxidants function as tumor promoters or cocarcinogens rather than as complete carcinogens perhaps because of the high levels of endogenous antioxidant defenses. It is also thought that oxidative damage in joints may trigger the autoimmune response that characterizes the persistence of the rheumatoid disease process. [NIH]

**Oxidation:** The act of oxidizing or state of being oxidized. Chemically it consists in the increase of positive charges on an atom or the loss of negative charges. Most biological oxidations are accomplished by the removal of a pair of hydrogen atoms (dehydrogenation) from a molecule. Such oxidations must be accompanied by reduction of an acceptor molecule. Univalent o. indicates loss of one electron; divalent o., the loss of two electrons. [EU]

**Oxidation-Reduction:** A chemical reaction in which an electron is transferred from one molecule to another. The electron-donating molecule is the reducing agent or reductant; the electron-accepting molecule is the oxidizing agent or oxidant. Reducing and oxidizing agents function as conjugate reductant-oxidant pairs or redox pairs (Lehninger, Principles of Biochemistry, 1982, p471). [NIH]

**Oxidative Stress:** A disturbance in the prooxidant-antioxidant balance in favor of the former, leading to potential damage. Indicators of oxidative stress include damaged DNA bases, protein oxidation products, and lipid peroxidation products (Sies, Oxidative Stress, 1991, pxv-xvi). [NIH]

**Oxygenation:** The process of supplying, treating, or mixing with oxygen. No:1245 - oxygenation the process of supplying, treating, or mixing with oxygen. [EU]

**Pachymeningitis:** Inflammation of the dura mater of the brain, the spinal cord or the optic nerve. [NIH]

**Paediatric:** Of or relating to the care and medical treatment of children; belonging to or concerned with paediatrics. [EU]

**Palliative:** 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

**Palsy:** Disease of the peripheral nervous system occurring usually after many years of increased lead absorption. [NIH]

**Pancreas:** A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

**Pancreatic:** Having to do with the pancreas. [NIH]

**Pancreatic cancer:** Cancer of the pancreas, a salivary gland of the abdomen. [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]

**Paranasal Sinuses:** Air-filled extensions of the respiratory part of the nasal cavity into the frontal, ethmoid, sphenoid, and maxillary cranial bones. They vary in size and form in different individuals and are lined by the ciliated mucous membranes of the nasal cavity. [NIH]

**Parasite:** An animal or a plant that lives on or in an organism of another species and gets at least some of its nutrition from that other organism. [NIH]

**Parenteral:** Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, etc. [EU]

**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]

**Particle Accelerators:** Devices which accelerate electrically charged atomic or subatomic particles, such as electrons, protons or ions, to high velocities so they have high kinetic energy. [NIH]

**Partnership Practice:** A voluntary contract between two or more doctors who may or may not share responsibility for the care of patients, with proportional sharing of profits and losses. [NIH]

**Parturition:** The act or process of given birth to a child. [EU]

**Passive transport:** The transport that occurs through the membrane at non-specific sites. [NIH]

**Pathogen:** Any disease-producing microorganism. [EU]

**Pathogenesis:** The cellular events and reactions that occur in the development of disease. [NIH]

**Pathologic:** 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

**Pathologic Processes:** The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

**Pathophysiology:** Altered functions in an individual or an organ due to disease. [NIH]

**Patient Education:** The teaching or training of patients concerning their own health needs. [NIH]

**Pediatrics:** A medical specialty concerned with maintaining health and providing medical care to children from birth to adolescence. [NIH]

**Pelvic:** Pertaining to the pelvis. [EU]

**Penicillin:** An antibiotic drug used to treat infection. [NIH]

**Penicillin Resistance:** Nonsusceptibility of an organism to the action of penicillins. [NIH]

**Penis:** The external reproductive organ of males. It is composed of a mass of erectile tissue enclosed in three cylindrical fibrous compartments. Two of the three compartments, the corpus cavernosa, are placed side-by-side along the upper part of the organ. The third compartment below, the corpus spongiosum, houses the urethra. [NIH]

**Pentoxifylline:** A methylxanthine derivative that inhibits phosphodiesterase and affects blood rheology. It improves blood flow by increasing erythrocyte and leukocyte flexibility. It also inhibits platelet aggregation. Pentoxifylline modulates immunologic activity by stimulating cytokine production. [NIH]

**Peptic:** Pertaining to pepsin or to digestion; related to the action of gastric juices. [EU]

**Peptide:** Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

**Peptide Chain Elongation:** The process whereby an amino acid is joined through a substituted amide linkage to a chain of peptides. [NIH]

**Peptide Hydrolases:** A subclass of enzymes from the hydrolase class that catalyze the hydrolysis of peptide bonds. Exopeptidases and endopeptidases make up the sub-subclasses for this group. EC 3.4. [NIH]

**Peptide Nucleic Acids:** DNA analogs containing neutral amide backbone linkages composed of aminoethyl glycine units instead of the usual phosphodiester linkage of deoxyribose groups. Peptide nucleic acids have high biological stability and higher affinity for complementary DNA or RNA sequences than analogous DNA oligomers. [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]

**Perianal:** Located around the anus. [EU]

**Pericoronitis:** Inflammation of the gingiva surrounding the crown of a tooth. [NIH]

**Perinatal:** Pertaining to or occurring in the period shortly before and after birth; variously defined as beginning with completion of the twentieth to twenty-eighth week of gestation and ending 7 to 28 days after birth. [EU]

**Perineal:** Pertaining to the perineum. [EU]

**Perineum:** The area between the anus and the sex organs. [NIH]

**Periodontal disease:** Disease involving the supporting structures of the teeth (as the gums and periodontal membranes). [NIH]

**Periodontitis:** Inflammation of the periodontal membrane; also called periodontitis simplex. [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]

**Periplasm:** The space between the inner and outer membranes of a cell that is shared with the cell wall. [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]

**Pesticides:** Chemicals used to destroy pests of any sort. The concept includes fungicides (industrial fungicides), insecticides, rodenticides, etc. [NIH]

**Petrolatum:** A colloidal system of semisolid hydrocarbons obtained from petroleum. It is used as an ointment base, topical protectant, and lubricant. [NIH]

**Petroleum:** Naturally occurring complex liquid hydrocarbons which, after distillation, yield combustible fuels, petrochemicals, and lubricants. [NIH]

**Phagocyte:** An immune system cell that can surround and kill microorganisms and remove dead cells. Phagocytes include macrophages. [NIH]

**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]

**Pharmaceutical Solutions:** Homogeneous liquid preparations that contain one or more chemical substances dissolved, i.e., molecularly dispersed, in a suitable solvent or mixture of mutually miscible solvents. For reasons of their ingredients, method of preparation, or use, they do not fall into another group of products. [NIH]

**Pharmacodynamic:** Is concerned with the response of living tissues to chemical stimuli, that is, the action of drugs on the living organism in the absence of disease. [NIH]

**Pharmacokinetic:** The mathematical analysis of the time courses of absorption, distribution, and elimination of drugs. [NIH]

**Pharmacologic:** Pertaining to pharmacology or to the properties and reactions of drugs. [EU]

**Pharyngitis:** Inflammation of the throat. [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]

**Phenolphthalein:** An acid-base indicator which is colorless in acid solution, but turns pink to red as the solution becomes alkaline. It is used medicinally as a cathartic. [NIH]

**Phenotype:** The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of yeasts. [NIH]

**Phenyl:** Ingredient used in cold and flu remedies. [NIH]

**Phosphodiesterase:** Effector enzyme that regulates the levels of a second messenger, the cyclic GMP. [NIH]

**Phospholipases:** A class of enzymes that catalyze the hydrolysis of phosphoglycerides or glycerophosphatidates. EC 3.1.-. [NIH]

**Phosphoric Monoester Hydrolases:** A group of hydrolases which catalyze the hydrolysis of monophosphoric esters with the production of one mole of orthophosphate. EC 3.1.3. [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]

**Phosphorylated:** Attached to a phosphate group. [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]

**Phosphotransferases:** A rather large group of enzymes comprising not only those transferring phosphate but also diphosphate, nucleotidyl residues, and others. These have also been subdivided according to the acceptor group. (From Enzyme Nomenclature, 1992) EC 2.7. [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]

**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]

**Piperacillin:** Semisynthetic, broad-spectrum, ampicillin-derived ureidopenicillin antibiotic proposed for pseudomonas infections. It is also used in combination with other antibiotics. [NIH]

**Piperidines:** A family of hexahydropyridines. Piperidine itself is found in the pepper plant as the alkaloid piperine. [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]

**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 protein:** One of the hundreds of different proteins present in blood plasma, including carrier proteins ( such albumin, transferrin, and haptoglobin), fibrinogen and other coagulation factors, complement components, immunoglobulins, enzyme inhibitors, precursors of substances such as angiotension and bradykinin, and many other types of proteins. [EU]

**Plasmid:** An autonomously replicating, extra-chromosomal DNA molecule found in many bacteria. Plasmids are widely used as carriers of cloned genes. [NIH]

**Plastids:** Self-replicating cytoplasmic organelles of plant and algal cells that contain pigments and may synthesize and accumulate various substances. Plastids are used in phylogenetic studies. [NIH]

**Platelet Activation:** A series of progressive, overlapping events triggered by exposure of the platelets to subendothelial tissue. These events include shape change, adhesiveness, aggregation, and release reactions. When carried through to completion, these events lead to the formation of a stable hemostatic plug. [NIH]

**Platelet Aggregation:** The attachment of platelets to one another. This clumping together can be induced by a number of agents (e.g., thrombin, collagen) and is part of the mechanism leading to the formation of a thrombus. [NIH]

**Platelets:** A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called thrombocytes. [NIH]

**Platinum:** Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

**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]

**Pleural Effusion:** Presence of fluid in the pleural cavity resulting from excessive transudation or exudation from the pleural surfaces. It is a sign of disease and not a diagnosis in itself. [NIH]

**Pneumococcal Infections:** Infections with bacteria of the species Streptococcus pneumoniae. [NIH]

**Pneumothorax:** Accumulation of air or gas in the space between the lung and chest wall, resulting in partial or complete collapse of the lung. [NIH]

**Podophyllotoxin:** The main active constituent of the resin from the roots of may apple or mandrake (Podophyllum peltatum and P. emodi). It is a potent spindle poison, toxic if taken internally, and has been used as a cathartic. It is very irritating to skin and mucous membranes, has keratolytic actions, has been used to treat warts and keratoses, and may have antineoplastic properties, as do some of its congeners and derivatives. [NIH]

**Poisoning:** A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

**Policy Making:** The decision process by which individuals, groups or institutions establish policies pertaining to plans, programs or procedures. [NIH]

**Polyesters:** Polymers of organic acids and alcohols, with ester linkages--usually polyethylene terephthalate; can be cured into hard plastic, films or tapes, or fibers which can be woven into fabrics, meshes or velours. [NIH]

**Polyethylene:** A vinyl polymer made from ethylene. It can be branched or linear. Branched or low-density polyethylene is tough and pliable but not to the same degree as linear polyethylene. Linear or high-density polyethylene has a greater hardness and tensile strength. Polyethylene is used in a variety of products, including implants and prostheses. [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]

**Polymers:** Compounds formed by the joining of smaller, usually repeating, units linked by

covalent bonds. These compounds often form large macromolecules (e.g., polypeptides, proteins, plastics). [NIH]

**Polymyxin:** Basic polypeptide antibiotic group obtained from Bacillus polymyxa. They affect the cell membrane by detergent action and may cause neuromuscular and kidney damage. At least eleven different members of the polymyxin group have been identified, each designated by a letter. [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]

**Polyproteins:** Proteins which are synthesized as a single polymer and then cleaved into several distinct proteins. [NIH]

**Polysaccharide:** A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

**Porosity:** Condition of having pores or open spaces. This often refers to bones, bone implants, or bone cements, but can refer to the porous state of any solid substance. [NIH]

**Port:** An implanted device through which blood may be withdrawn and drugs may be infused without repeated needle sticks. Also called a port-a-cath. [NIH]

**Port-a-cath:** An implanted device through which blood may be withdrawn and drugs may be infused without repeated needle sticks. Also called a port. [NIH]

**Portal Vein:** A short thick vein formed by union of the superior mesenteric vein and the splenic vein. [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]

**Postoperative:** After surgery. [NIH]

**Postoperative Complications:** Pathologic processes that affect patients after a surgical procedure. They may or may not be related to the disease for which the surgery was done, and they may or may not be direct results of the surgery. [NIH]

**Postsynaptic:** Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

**Post-translational:** The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [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]

**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]

**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]

**Prepuce:** A covering fold of skin; often used alone to designate the preputium penis. [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]

**Primary Prevention:** Prevention of disease or mental disorders in susceptible individuals or populations through promotion of health, including mental health, and specific protection, as in immunization, as distinguished from the prevention of complications or after-effects of existing disease. [NIH]

**Private Practice:** Practice of a health profession by an individual, offering services on a person-to-person basis, as opposed to group or partnership practice. [NIH]

**Probe:** An instrument used in exploring cavities, or in the detection and dilatation of strictures, or in demonstrating the potency of channels; an elongated instrument for exploring or sounding body cavities. [NIH]

**Procaine:** A local anesthetic of the ester type that has a slow onset and a short duration of action. It is mainly used for infiltration anesthesia, peripheral nerve block, and spinal block. (From Martindale, The Extra Pharmacopoeia, 30th ed, p1016). [NIH]

**Prodigiosin:** 4-Methoxy-5-((5-methyl-4-pentyl-2H-pyrrol-2-ylidene)methyl)- 2,2'-bi-1H-pyrrole. A toxic, bright red tripyrrole pigment from Serratia marcescens and others. It has antibacterial, anticoccidial, antimalarial, and antifungal activities, but is used mainly as a biochemical tool. [NIH]

**Prodrug:** A substance that gives rise to a pharmacologically active metabolite, although not itself active (i. e. an inactive precursor). [NIH]

**Progeny:** The offspring produced in any generation. [NIH]

**Progesterone:** Pregn-4-ene-3,20-dione. The principal progestational hormone of the body, secreted by the corpus luteum, adrenal cortex, and placenta. Its chief function is to prepare the uterus for the reception and development of the fertilized ovum. It acts as an antiovulatory agent when administered on days 5-25 of the menstrual cycle. [NIH]

**Progression:** Increase in the size of a tumor or spread of cancer in the body. [NIH]

**Progressive:** Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

**Projection:** A defense mechanism, operating unconsciously, whereby that which is emotionally unacceptable in the self is rejected and attributed (projected) to others. [NIH]

**Proline:** A non-essential amino acid that is synthesized from glutamic acid. It is an essential component of collagen and is important for proper functioning of joints and tendons. [NIH]

**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]

**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]

**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]

**Propylene Glycol:** A clear, colorless, viscous organic solvent and diluent used in pharmaceutical preparations. [NIH]

**Prospective study:** An epidemiologic study in which a group of individuals (a cohort), all free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

**Prostaglandin:** Any of a group of components derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway that are extremely potent mediators of a diverse group of physiologic processes. The abbreviation for prostaglandin is PG; specific compounds are designated by adding one of the letters A through I to indicate the type of substituents found on the hydrocarbon skeleton and a subscript (1, 2 or 3) to indicate the number of double bonds in the hydrocarbon skeleton e.g., PGE2. The predominant naturally occurring prostaglandins all have two double bonds and are synthesized from arachidonic acid (5,8,11,14-eicosatetraenoic acid) by the pathway shown in the illustration. The 1 series and 3 series are produced by the same pathway with fatty acids having one fewer double bond (8,11,14-eicosatrienoic acid or one more double bond (5,8,11,14,17-eicosapentaenoic acid) than arachidonic acid. The subscript a or ß indicates the configuration at C-9 (a denotes a substituent below the plane of the ring, ß, above the plane). The naturally occurring PGF's have the a configuration, e.g., PGF2a. All of the prostaglandins act by binding to specific cell-surface receptors causing an increase in the level of the intracellular second messenger cyclic AMP (and in some cases cyclic GMP also). The effect produced by the cyclic AMP increase depends on the specific cell type. In some cases there is also a positive feedback effect. Increased cyclic AMP increases prostaglandin synthesis leading to further increases in cyclic AMP. [EU]

**Prostaglandin-Endoperoxide Synthase:** An enzyme complex that catalyzes the formation of prostaglandins from the appropriate unsaturated fatty acid, molecular oxygen, and a reduced acceptor. EC 1.14.99.1. [NIH]

**Prostaglandins A:** (13E,15S)-15-Hydroxy-9-oxoprosta-10,13-dien-1-oic acid (PGA(1)); (5Z,13E,15S)-15-hydroxy-9-oxoprosta-5,10,13-trien-1-oic acid (PGA(2)); (5Z,13E,15S,17Z)-15-hydroxy-9-oxoprosta-5,10,13,17-tetraen-1-oic acid (PGA(3)). A group of naturally occurring secondary prostaglandins derived from PGE. PGA(1) and PGA(2) as well as their 19-hydroxy derivatives are found in many organs and tissues. [NIH]

**Prostate:** A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

**Prostate gland:** A gland in the male reproductive system just below the bladder. It surrounds part of the urethra, the canal that empties the bladder, and produces a fluid that forms part of semen. [NIH]

**Prostatitis:** Inflammation of the prostate. [EU]

**Prosthesis:** An artificial replacement of a part of the body. [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 C:** A vitamin-K dependent zymogen present in the blood, which, upon activation by thrombin and thrombomodulin exerts anticoagulant properties by inactivating factors Va and VIIIa at the rate-limiting steps of thrombin formation. [NIH]

**Protein Conformation:** The characteristic 3-dimensional shape of a protein, including the secondary, supersecondary (motifs), tertiary (domains) and quaternary structure of the peptide chain. Quaternary protein structure describes the conformation assumed by multimeric proteins (aggregates of more than one polypeptide chain). [NIH]

**Protein Engineering:** Procedures by which nonrandom single-site changes are introduced into structural genes (site-specific mutagenesis) in order to produce mutant genes which can be coupled to promoters that direct the synthesis of a specifically altered protein, which is then analyzed for structural and functional properties and then compared with the predicted and sought-after properties. The design of the protein may be assisted by computer graphic technology and other advanced molecular modeling techniques. [NIH]

**Protein S:** The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

**Proteins:** Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

**Proteinuria:** The presence of protein in the urine, indicating that the kidneys are not working properly. [NIH]

**Proteoglycans:** Glycoproteins which have a very high polysaccharide content. [NIH]

**Proteolytic:** 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

**Prothrombin:** A plasma protein that is the inactive precursor of thrombin. It is converted to thrombin by a prothrombin activator complex consisting of factor Xa, factor V, phospholipid, and calcium ions. Deficiency of prothrombin leads to hypoprothrombinemia. [NIH]

**Protocol:** The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other aspects of trial design. [NIH]

**Protons:** Stable elementary particles having the smallest known positive charge, found in the nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

**Protozoa:** A subkingdom consisting of unicellular organisms that are the simplest in the animal kingdom. Most are free living. They range in size from submicroscopic to macroscopic. Protozoa are divided into seven phyla: Sarcomastigophora, Labyrinthomorpha, Apicomplexa, Microspora, Ascetospora, Myxozoa, and Ciliophora. [NIH]

**Proximal:** Nearest; closer to any point of reference; opposed to distal. [EU]

**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]

**Pseudomonas:** A genus of gram-negative, aerobic, rod-shaped bacteria widely distributed in nature. Some species are pathogenic for humans, animals, and plants. [NIH]

**Pseudomonas Infections:** Infections with bacteria of the genus Pseudomonas. [NIH]

**Psychosis:** A mental disorder characterized by gross impairment in reality testing as evidenced by delusions, hallucinations, markedly incoherent speech, or disorganized and agitated behaviour without apparent awareness on the part of the patient of the incomprehensibility of his behaviour; the term is also used in a more general sense to refer to mental disorders in which mental functioning is sufficiently impaired as to interfere grossly with the patient's capacity to meet the ordinary demands of life. Historically, the term has been applied to many conditions, e.g. manic-depressive psychosis, that were first described in psychotic patients, although many patients with the disorder are not judged psychotic. [EU]

**Puberty:** The period during which the secondary sex characteristics begin to develop and the capability of sexual reproduction is attained. [EU]

**Public Health:** Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the international, national, state, or municipal level. [NIH]

**Public Policy:** A course or method of action selected, usually by a government, from among alternatives to guide and determine present and future decisions. [NIH]

**Publishing:** "The business or profession of the commercial production and issuance of literature" (Webster's 3d). It includes the publisher, publication processes, editing and editors. Production may be by conventional printing methods or by electronic publishing. [NIH]

**Puerperium:** Period from delivery of the placenta until return of the reproductive organs to their normal nonpregnant morphologic state. In humans, the puerperium generally lasts for six to eight weeks. [NIH]

**Pulmonary:** Relating to the lungs. [NIH]

**Pulmonary Embolism:** Embolism in the pulmonary artery or one of its branches. [NIH]

**Pulposus:** Prolapse of the nucleus pulposus into the body of the vertebra; necrobacillosis of rabbits. [NIH]

**Pulse:** The rhythmical expansion and contraction of an artery produced by waves of pressure caused by the ejection of blood from the left ventricle of the heart as it contracts. [NIH]

**Pupil:** The aperture in the iris through which light passes. [NIH]

**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]

**Purulent:** Consisting of or containing pus; associated with the formation of or caused by pus. [EU]

**Pustular:** Pertaining to or of the nature of a pustule; consisting of pustules (= a visible collection of pus within or beneath the epidermis). [EU]

**Pyelonephritis:** Inflammation of the kidney and its pelvis, beginning in the interstitium and rapidly extending to involve the tubules, glomeruli, and blood vessels; due to bacterial

infection. [EU]

**Pyogenic:** Producing pus; pyopoietic (= liquid inflammation product made up of cells and a thin fluid called liquor puris). [EU]

**Quality of Life:** A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

**Quinidine:** An optical isomer of quinine, extracted from the bark of the Cinchona tree and similar plant species. This alkaloid dampens the excitability of cardiac and skeletal muscles by blocking sodium and potassium currents across cellular membranes. It prolongs cellular action potential, and decreases automaticity. Quinidine also blocks muscarinic and alpha-adrenergic neurotransmission. [NIH]

**Quinine:** An alkaloid derived from the bark of the cinchona tree. It is used as an antimalarial drug, and is the active ingredient in extracts of the cinchona that have been used for that purpose since before 1633. Quinine is also a mild antipyretic and analgesic and has been used in common cold preparations for that purpose. It was used commonly and as a bitter and flavoring agent, and is still useful for the treatment of babesiosis. Quinine is also useful in some muscular disorders, especially nocturnal leg cramps and myotonia congenita, because of its direct effects on muscle membrane and sodium channels. The mechanisms of its antimalarial effects are not well understood. [NIH]

**Race:** A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

**Radiation:** Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

**Radioactive:** Giving off radiation. [NIH]

**Radiological:** Pertaining to radiodiagnostic and radiotherapeutic procedures, and interventional radiology or other planning and guiding medical radiology. [NIH]

**Radiologist:** A doctor who specializes in creating and interpreting pictures of areas inside the body. The pictures are produced with x-rays, sound waves, or other types of energy. [NIH]

**Radiology:** A specialty concerned with the use of x-ray and other forms of radiant energy in the diagnosis and treatment of disease. [NIH]

**Radius:** The lateral bone of the forearm. [NIH]

**Random Allocation:** A process involving chance used in therapeutic trials or other research endeavor for allocating experimental subjects, human or animal, between treatment and control groups, or among treatment groups. It may also apply to experiments on inanimate objects. [NIH]

**Randomization:** Also called random allocation. Is allocation of individuals to groups, e.g., for experimental and control regimens, by chance. Within the limits of chance variation, random allocation should make the control and experimental groups similar at the start of an investigation and ensure that personal judgment and prejudices of the investigator do not influence allocation. [NIH]

**Randomized:** Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

**Randomized Controlled Trials:** Clinical trials that involve at least one test treatment and one control treatment, concurrent enrollment and follow-up of the test- and control-treated groups, and in which the treatments to be administered are selected by a random process,

such as the use of a random-numbers table. Treatment allocations using coin flips, odd-even numbers, patient social security numbers, days of the week, medical record numbers, or other such pseudo- or quasi-random processes, are not truly randomized and trials employing any of these techniques for patient assignment are designated simply controlled clinical trials. [NIH]

**Ranitidine:** A non-imidazole blocker of those histamine receptors that mediate gastric secretion (H2 receptors). It is used to treat gastrointestinal ulcers. [NIH]

**Ranitidine Bismuth Citrate:** Drug used to eradicate Helicobacter pylori. [NIH]

**Reagent:** A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

**Reality Testing:** The individual's objective evaluation of the external world and the ability to differentiate adequately between it and the internal world; considered to be a primary ego function. [NIH]

**Receptor:** A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

**Recombinant:** A cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

**Recombinant Proteins:** Proteins prepared by recombinant DNA technology. [NIH]

**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]

**Refer:** To send or direct for treatment, aid, information, de decision. [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]

**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]

**Renin:** An enzyme which is secreted by the kidney and is formed from prorenin in plasma and kidney. The enzyme cleaves the Leu-Leu bond in angiotensinogen to generate angiotensin I. EC 3.4.23.15. (Formerly EC 3.4.99.19). [NIH]

**Renin-Angiotensin System:** A system consisting of renin, angiotensin-converting enzyme, and angiotensin II. Renin, an enzyme produced in the kidney, acts on angiotensinogen, an alpha-2 globulin produced by the liver, forming angiotensin I. The converting enzyme contained in the lung acts on angiotensin I in the plasma converting it to angiotensin II, the most powerful directly pressor substance known. It causes contraction of the arteriolar smooth muscle and has other indirect actions mediated through the adrenal cortex. [NIH]

**Repressor:** Any of the specific allosteric protein molecules, products of regulator genes, which bind to the operator of operons and prevent RNA polymerase from proceeding into the operon to transcribe messenger RNA. [NIH]

**Resident physician:** A physician who lives in a hospital and is constantly available, as an intern. [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 Burst:** A large increase in oxygen uptake by neutrophils and most types of tissue macrophages through activation of an NADPH-cytochrome b-dependent oxidase that reduces oxygen to a superoxide. Individuals with an inherited defect in which the oxidase that reduces oxygen to superoxide is decreased or absent (granulomatous disease, chronic) often die as a result of recurrent bacterial infections. [NIH]

**Respiratory distress syndrome:** A lung disease that occurs primarily in premature infants; the newborn must struggle for each breath and blueing of its skin reflects the baby's inability to get enough oxygen. [NIH]

**Respiratory failure:** Inability of the lungs to conduct gas exchange. [NIH]

**Response Elements:** Nucleotide sequences, usually upstream, which are recognized by specific regulatory transcription factors, thereby causing gene response to various regulatory agents. These elements may be found in both promotor and enhancer regions. [NIH]

**Restoration:** Broad term applied to any inlay, crown, bridge or complete denture which restores or replaces loss of teeth or oral tissues. [NIH]

**Retina:** The ten-layered nervous tissue membrane of the eye. It is continuous with the optic nerve and receives images of external objects and transmits visual impulses to the brain. Its outer surface is in contact with the choroid and the inner surface with the vitreous body. The outer-most layer is pigmented, whereas the inner nine layers are transparent. [NIH]

**Retinal:** 1. Pertaining to the retina. 2. The aldehyde of retinol, derived by the oxidative enzymatic splitting of absorbed dietary carotene, and having vitamin A activity. In the retina, retinal combines with opsins to form visual pigments. One isomer, 11-cis retinal combines with opsin in the rods (scotopsin) to form rhodopsin, or visual purple. Another,

all-trans retinal (trans-r.); visual yellow; xanthopsin) results from the bleaching of rhodopsin by light, in which the 11-cis form is converted to the all-trans form. Retinal also combines with opsins in the cones (photopsins) to form the three pigments responsible for colour vision. Called also retinal, and retinene1. [EU]

**Retinitis:** Inflammation of the retina. It is rarely limited to the retina, but is commonly associated with diseases of the choroid (chorioretinitis) and of the optic nerve (neuroretinitis). The disease may be confined to one eye, but since it is generally dependent on a constitutional factor, it is almost always bilateral. It may be acute in course, but as a rule it lasts many weeks or even several months. [NIH]

**Retinoid:** Vitamin A or a vitamin A-like compound. [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]

**Retrospective:** Looking back at events that have already taken place. [NIH]

**Retrovirus:** A member of a group of RNA viruses, the RNA of which is copied during viral replication into DNA by reverse transcriptase. The viral DNA is then able to be integrated into the host chromosomal DNA. [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]

**Rheology:** The study of the deformation and flow of matter, usually liquids or fluids, and of the plastic flow of solids. The concept covers consistency, dilatancy, liquefaction, resistance to flow, shearing, thixotrophy, and viscosity. [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]

**Riboflavin:** Nutritional factor found in milk, eggs, malted barley, liver, kidney, heart, and leafy vegetables. The richest natural source is yeast. It occurs in the free form only in the retina of the eye, in whey, and in urine; its principal forms in tissues and cells are as FMN and FAD. [NIH]

**Ribonucleic acid:** RNA. One of the two nucleic acids found in all cells. The other is deoxyribonucleic acid (DNA). Ribonucleic acid transfers genetic information from DNA to proteins produced by the cell. [NIH]

**Ribonucleoproteins:** Proteins conjugated with ribonucleic acids (RNA) or specific RNA. Many viruses are ribonucleoproteins. [NIH]

**Ribose:** A pentose active in biological systems usually in its D-form. [NIH]

**Ribosome:** A granule of protein and RNA, synthesized in the nucleolus and found in the cytoplasm of cells. Ribosomes are the main sites of protein synthesis. Messenger RNA attaches to them and there receives molecules of transfer RNA bearing amino acids. [NIH]

**Rigidity:** Stiffness or inflexibility, chiefly that which is abnormal or morbid; rigor. [EU]

**Risk factor:** A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

**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]

**RNA:** Ribonucleic acid. One of the two types of nucleic acids found in cells. The other is DNA (deoxyribonucleic acid). RNA plays a role in sending information from DNA to the protein-forming system of the cell. [NIH]

**Rod:** A reception for vision, located in the retina. [NIH]

**Rodenticides:** Substances used to destroy or inhibit the action of rats, mice, or other rodents. [NIH]

**Root Planing:** A procedure for smoothing of the roughened root surface or cementum of a tooth after subgingival curettage or scaling, as part of periodontal therapy. [NIH]

**Saccharomyces:** A genus of ascomycetous fungi of the family Saccharomycetaceae, order saccharomycetales. [NIH]

**Saccharomycetales:** An order of fungi in the phylum Ascomycota that multiply by budding. They include the telomorphic ascomycetous yeasts which are found in a very wide range of habitats. [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]

**Salmonellosis:** Infection by salmonellae. [NIH]

**Saponins:** Sapogenin glycosides. A type of glycoside widely distributed in plants. Each consists of a sapogenin as the aglycon moiety, and a sugar. The sapogenin may be a steroid or a triterpene and the sugar may be glucose, galactose, a pentose, or a methylpentose. Sapogenins are poisonous towards the lower forms of life and are powerful hemolytics when injected into the blood stream able to dissolve red blood cells at even extreme dilutions. [NIH]

**Scans:** Pictures of structures inside the body. Scans often used in diagnosing, staging, and monitoring disease include liver scans, bone scans, and computed tomography (CT) or computerized axial tomography (CAT) scans and magnetic resonance imaging (MRI) scans. In liver scanning and bone scanning, radioactive substances that are injected into the bloodstream collect in these organs. A scanner that detects the radiation is used to create pictures. In CT scanning, an x-ray machine linked to a computer is used to produce detailed pictures of organs inside the body. MRI scans use a large magnet connected to a computer to create pictures of areas inside the body. [NIH]

**Schizoid:** Having qualities resembling those found in greater degree in schizophrenics; a person of schizoid personality. [NIH]

**Schizophrenia:** A mental disorder characterized by a special type of disintegration of the personality. [NIH]

**Schizotypal Personality Disorder:** A personality disorder in which there are oddities of thought (magical thinking, paranoid ideation, suspiciousness), perception (illusions, depersonalization), speech (digressive, vague, overelaborate), and behavior (inappropriate affect in social interactions, frequently social isolation) that are not severe enough to characterize schizophrenia. [NIH]

**Sclera:** The tough white outer coat of the eyeball, covering approximately the posterior five-sixths of its surface, and continuous anteriorly with the cornea and posteriorly with the

external sheath of the optic nerve. [EU]

**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]

**Sebaceous gland:** Gland that secretes sebum. [NIH]

**Sebum:** The oily substance secreted by sebaceous glands. It is composed of keratin, fat, and cellular debris. [NIH]

**Second Messenger Systems:** Systems in which an intracellular signal is generated in response to an intercellular primary messenger such as a hormone or neurotransmitter. They are intermediate signals in cellular processes such as metabolism, secretion, contraction, phototransduction, and cell growth. Examples of second messenger systems are the adenyl cyclase-cyclic AMP system, the phosphatidylinositol diphosphate-inositol triphosphate system, and the cyclic GMP system. [NIH]

**Secretion:** 1. The process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. Any substance produced by secretion. [EU]

**Segregation:** The separation in meiotic cell division of homologous chromosome pairs and their contained allelomorphic gene pairs. [NIH]

**Seizures:** Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena. Recurrent seizures are usually referred to as epilepsy or "seizure disorder." [NIH]

**Selenium:** An element with the atomic symbol Se, atomic number 34, and atomic weight 78.96. It is an essential micronutrient for mammals and other animals but is toxic in large amounts. Selenium protects intracellular structures against oxidative damage. It is an essential component of glutathione peroxidase. [NIH]

**Semen:** The thick, yellowish-white, viscid fluid secretion of male reproductive organs discharged upon ejaculation. In addition to reproductive organ secretions, it contains spermatozoa and their nutrient plasma. [NIH]

**Semicircular canal:** Three long canals of the bony labyrinth of the ear, forming loops and opening into the vestibule by five openings. [NIH]

**Semisynthetic:** Produced by chemical manipulation of naturally occurring substances. [EU]

**Sensor:** A device designed to respond to physical stimuli such as temperature, light, magnetism or movement and transmit resulting impulses for interpretation, recording, movement, or operating control. [NIH]

**Sepsis:** The presence of bacteria in the bloodstream. [NIH]

**Septal:** An abscess occurring at the root of the tooth on the proximal surface. [NIH]

**Septic:** Produced by or due to decomposition by microorganisms; putrefactive. [EU]

**Septicemia:** Systemic disease associated with the presence and persistence of pathogenic microorganisms or their toxins in the blood. Called also blood poisoning. [EU]

**Septum:** A dividing wall or partition; a general term for such a structure. The term is often used alone to refer to the septal area or to the septum pellucidum. [EU]

**Septum Pellucidum:** A triangular double membrane separating the anterior horns of the lateral ventricles of the brain. It is situated in the median plane and bounded by the corpus

callosum and the body and columns of the fornix. [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]

**Serine:** A non-essential amino acid occurring in natural form as the L-isomer. It is synthesized from glycine or threonine. It is involved in the biosynthesis of purines, pyrimidines, and other amino acids. [NIH]

**Serotonin:** A biochemical messenger and regulator, synthesized from the essential amino acid L-tryptophan. In humans it is found primarily in the central nervous system, gastrointestinal tract, and blood platelets. Serotonin mediates several important physiological functions including neurotransmission, gastrointestinal motility, hemostasis, and cardiovascular integrity. Multiple receptor families (receptors, serotonin) explain the broad physiological actions and distribution of this biochemical mediator. [NIH]

**Serous:** Having to do with serum, the clear liquid part of blood. [NIH]

**Serum:** The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

**Sex Characteristics:** Those characteristics that distinguish one sex from the other. The primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

**Sexually Transmitted Diseases:** Diseases due to or propagated by sexual contact. [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]

**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]

**Shunt:** A surgically created diversion of fluid (e.g., blood or cerebrospinal fluid) from one area of the body to another area of the body. [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]

**Sigma Factor:** A protein which is a subunit of RNA polymerase. It effects initiation of specific RNA chains from DNA. [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]

**Skin graft:** Skin that is moved from one part of the body to another. [NIH]

**Skin Tests:** Epicutaneous or intradermal application of a sensitizer for demonstration of either delayed or immediate hypersensitivity. Used in diagnosis of hypersensitivity or as a test for cellular immunity. [NIH]

**Skull:** The skeleton of the head including the bones of the face and the bones enclosing the brain. [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]

**Soaps:** Sodium or potassium salts of long chain fatty acids. These detergent substances are obtained by boiling natural oils or fats with caustic alkali. Sodium soaps are harder and are used as topical anti-infectives and vehicles in pills and liniments; potassium soaps are soft, used as vehicles for ointments and also as topical antimicrobials. [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]

**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]

**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]

**Sound wave:** An alteration of properties of an elastic medium, such as pressure, particle displacement, or density, that propagates through the medium, or a superposition of such

alterations. [NIH]

**Specialist:** In medicine, one who concentrates on 1 special branch of medical science. [NIH]

**Species:** A taxonomic category subordinate to a genus (or subgenus) and superior to a subspecies or variety, composed of individuals possessing common characters distinguishing them from other categories of individuals of the same taxonomic level. In taxonomic nomenclature, species are designated by the genus name followed by a Latin or Latinized adjective or noun. [EU]

**Specificity:** Degree of selectivity shown by an antibody with respect to the number and types of antigens with which the antibody combines, as well as with respect to the rates and the extents of these reactions. [NIH]

**Spectrum:** A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

**Speculum:** An instrument used to widen an opening of the body to make it easier to look inside. [NIH]

**Sperm:** The fecundating fluid of the male. [NIH]

**Spermatozoa:** Mature male germ cells that develop in the seminiferous tubules of the testes. Each consists of a head, a body, and a tail that provides propulsion. The head consists mainly of chromatin. [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 Nerves:** The 31 paired peripheral nerves formed by the union of the dorsal and ventral spinal roots from each spinal cord segment. The spinal nerve plexuses and the spinal roots are also included. [NIH]

**Spiramycin:** A macrolide antibiotic produced by Streptomyces ambofaciens. The drug is effective against gram-positive aerobic pathogens, N. gonorrhoeae, and staphylococci. It is used to treat infections caused by bacteria and Toxoplasma gondii. [NIH]

**Splenic Vein:** Vein formed by the union (at the hilus of the spleen) of several small veins from the stomach, pancreas, spleen and mesentery. [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]

**Stabilization:** The creation of a stable state. [EU]

**Staging:** Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

**Staphylocoagulase:** A substance produced by pathogenic strains of staphylococci, which has the property of coagulating human or rabbit plasma. [NIH]

**Staphylococcus:** A genus of gram-positive, facultatively anaerobic, coccoid bacteria. Its organisms occur singly, in pairs, and in tetrads and characteristically divide in more than

one plane to form irregular clusters. Natural populations of Staphylococcus are membranes of warm-blooded animals. Some species are opportunistic pathogens of humans and animals. [NIH]

**Status Epilepticus:** Repeated and prolonged epileptic seizures without recovery of consciousness between attacks. [NIH]

**Steady state:** Dynamic equilibrium. [EU]

**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]

**Stent:** A device placed in a body structure (such as a blood vessel or the gastrointestinal tract) to provide support and keep the structure open. [NIH]

**Sterile:** Unable to produce children. [NIH]

**Sterility:** 1. The inability to produce offspring, i.e., the inability to conceive (female s.) or to induce conception (male s.). 2. The state of being aseptic, or free from microorganisms. [EU]

**Sterilization:** The destroying of all forms of life, especially microorganisms, by heat, chemical, or other means. [NIH]

**Sternum:** Breast bone. [NIH]

**Steroid:** A group name for lipids that contain a hydrogenated cyclopentanoperhydrophenanthrene ring system. Some of the substances included in this group are progesterone, adrenocortical hormones, the gonadal hormones, cardiac aglycones, bile acids, sterols (such as cholesterol), toad poisons, saponins, and some of the carcinogenic hydrocarbons. [EU]

**Stimulant:** 1. Producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. An agent or remedy that produces stimulation. [EU]

**Stimulus:** That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

**Stoma:** A surgically created opening from an area inside the body to the outside. [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]

**Streptococci:** A genus of spherical Gram-positive bacteria occurring in chains or pairs. They are widely distributed in nature, being important pathogens but often found as normal commensals in the mouth, skin, and intestine of humans and other animals. [NIH]

**Streptomyces:** A genus of bacteria that form a nonfragmented aerial mycelium. Many species have been identified with some being pathogenic. This genus is responsible for producing a majority of the antibiotics of practical value. [NIH]

**Streptomycin:** O-2-Deoxy-2-(methylamino)-alpha-L-glucopyranosyl-(1-2)-O-5- deoxy-3-C-formyl-alpha-L-lyxofuranosyl-(1-4)-N,N'-bis- (aminoiminomethyl)-D-streptamine. Antibiotic substance produced by the soil actinomycete Streptomyces griseus. It acts by inhibiting the initiation and elongation processes during protein synthesis. [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]

**Striatum:** A higher brain's domain thus called because of its stripes. [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]

**Stromal:** Large, veil-like cell in the bone marrow. [NIH]

**Structure-Activity Relationship:** The relationship between the chemical structure of a compound and its biological or pharmacological activity. Compounds are often classed together because they have structural characteristics in common including shape, size, stereochemical arrangement, and distribution of functional groups. Other factors contributing to structure-activity relationship include chemical reactivity, electronic effects, resonance, and inductive effects. [NIH]

**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]

**Subconjunctival:** Situated or occurring beneath the conjunctiva. [EU]

**Subcutaneous:** Beneath the skin. [NIH]

**Subspecies:** A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

**Substance P:** An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

**Substrate:** A substance upon which an enzyme acts. [EU]

**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]

**Sulfisoxazole:** One of the antibacterial sulfonamides generally used for treatment of infections. It is bacteriostatic against a wide range of gram- negative and gram-positive organisms, but acquired resistance is common. [NIH]

**Sulfur:** An element that is a member of the chalcogen family. It has an atomic symbol S, atomic number 16, and atomic weight 32.066. It is found in the amino acids cysteine and methionine. [NIH]

**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]

**Superoxide:** Derivative of molecular oxygen that can damage cells. [NIH]

**Suppurative:** Consisting of, containing, associated with, or identified by the formation of

pus. [NIH]

**Surface Plasmon Resonance:** A biosensing technique in which biomolecules capable of binding to specific analytes or ligands are first immobilized on one side of a metallic film. Light is then focused on the opposite side of the film to excite the surface plasmons, that is, the oscillations of free electrons propagating along the film's surface. The refractive index of light reflecting off this surface is measured. When the immobilized biomolecules are bound by their ligands, an alteration in surface plasmons on the opposite side of the film is created which is directly proportional to the change in bound, or adsorbed, mass. Binding is measured by changes in the refractive index. The technique is used to study biomolecular interactions, such as antigen-antibody binding. [NIH]

**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]

**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]

**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]

**Synchrotron:** An accelerator in which the particles are guided by an increasing magnetic field while they are accelerated several times in an approximately circular path by electric fields produced by a high-frequency generator. [NIH]

**Synergistic:** Acting together; enhancing the effect of another force or agent. [EU]

**Systemic:** Affecting the entire body. [NIH]

**Systemic disease:** Disease that affects the whole body. [NIH]

**Tachycardia:** Excessive rapidity in the action of the heart, usually with a heart rate above 100 beats per minute. [NIH]

**Tachypnea:** Rapid breathing. [NIH]

**Taurine:** 2-Aminoethanesulfonic acid. A conditionally essential nutrient, important during mammalian development. It is present in milk but is isolated mostly from ox bile and strongly conjugates bile acids. [NIH]

**Tear Gases:** Gases that irritate the eyes, throat, or skin. Severe lacrimation develops upon irritation of the eyes. [NIH]

**Teichoic Acids:** Bacterial polysaccharides that are rich in phosphodiester linkages. They are the major components of the cell walls and membranes of many bacteria. [NIH]

**Teicoplanin:** Glycopeptide antibiotic complex from Actinoplanes teichomyceticus active against gram-positive bacteria. It consists of five major components each with a different fatty acid moiety. [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]

**Teratogenic:** Tending to produce anomalies of formation, or teratism (= anomaly of formation or development : condition of a monster). [EU]

**Terminator:** A DNA sequence sited at the end of a transcriptional unit that signals the end of transcription. [NIH]

**Testicular:** Pertaining to a testis. [EU]

**Testis:** Either of the paired male reproductive glands that produce the male germ cells and the male hormones. [NIH]

**Tetracycline:** An antibiotic originally produced by Streptomyces viridifaciens, but used mostly in synthetic form. It is an inhibitor of aminoacyl-tRNA binding during protein synthesis. [NIH]

**Tetracycline Resistance:** Nonsusceptibility of a microbe (usually a bacterium) to the action of tetracycline, which binds to the 30S ribosomal subunit and prevents the normal binding of aminoacyl-tRNA. [NIH]

**Thalidomide:** A pharmaceutical agent originally introduced as a non-barbiturate hypnotic, but withdrawn from the market because of its known tetratogenic effects. It has been reintroduced and used for a number of immunological and inflammatory disorders. Thalidomide displays immunosuppresive and anti-angiogenic activity. It inhibits release of tumor necrosis factor alpha from monocytes, and modulates other cytokine action. [NIH]

**Theophylline:** Alkaloid obtained from Thea sinensis (tea) and others. It stimulates the heart and central nervous system, dilates bronchi and blood vessels, and causes diuresis. The drug is used mainly in bronchial asthma and for myocardial stimulation. Among its more prominent cellular effects are inhibition of cyclic nucleotide phosphodiesterases and antagonism of adenosine receptors. [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]

**Thiamine:** 3-((4-Amino-2-methyl-5-pyrimidinyl)methyl)-5-(2-hydroxyethyl)-4-methylthiazolium chloride. [NIH]

**Thiostrepton:** Polypeptide-containing antibiotic isolated from a species of Streptomyces in New Mexican soil. It appears to be highly active against gram-positive bacteria. In veterinary medicine, thiostrepton has been used in mastitis caused by gram-negative organisms and in dermatologic disorders. [NIH]

**Thoracostomy:** Surgical creation of an opening (stoma) into the chest cavity for drainage; used in the treatment of pleural effusion, pneumothorax, hemothorax and empyema. [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]

**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]

**Thrombomodulin:** A cell surface glycoprotein of endothelial cells that binds thrombin and serves as a cofactor in the activation of protein C and its regulation of blood coagulation. [NIH]

**Thrombosis:** The formation or presence of a blood clot inside a blood vessel. [NIH]

**Thromboxanes:** Physiologically active compounds found in many organs of the body. They are formed in vivo from the prostaglandin endoperoxides and cause platelet aggregation, contraction of arteries, and other biological effects. Thromboxanes are important mediators of the actions of polyunsaturated fatty acids transformed by cyclooxygenase. [NIH]

**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]

**Tin:** A trace element that is required in bone formation. It has the atomic symbol Sn, atomic number 50, and atomic weight 118.71. [NIH]

**Tin Compounds:** Inorganic compounds that contain tin as an integral part of the molecule. [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]

**Tobramycin:** An aminoglycoside, broad-spectrum antibiotic produced by Streptomyces tenebrarius. It is effective against gram-negative bacteria, especially the Pseudomonas species. It is a 10% component of the antibiotic complex, nebramycin, produced by the same species. [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]

**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]

**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]

**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]

**Trachoma:** A chronic infection of the conjunctiva and cornea caused by Chlamydia trachomatis. [NIH]

**Traction:** The act of pulling. [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]

**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]

**Transfusion:** The infusion of components of blood or whole blood into the bloodstream. The blood may be donated from another person, or it may have been taken from the person earlier and stored until needed. [NIH]

**Translation:** The process whereby the genetic information present in the linear sequence of ribonucleotides in mRNA is converted into a corresponding sequence of amino acids in a protein. It occurs on the ribosome and is unidirectional. [NIH]

**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]

**Transposons:** Discrete genetic elements capable of inserting, in a non-permuted fashion, into the chromosomes of many bacteria. [NIH]

**Trauma:** Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [NIH]

**Treatment Failure:** A measure of the quality of health care by assessment of unsuccessful results of management and procedures used in combating disease, in individual cases or series. [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]

**Triclosan:** A diphenyl ether derivative used in cosmetics and toilet soaps as an antiseptic. It has some bacteriostatic and fungistatic action. [NIH]

**Trimethoprim-sulfamethoxazole:** An antibiotic drug used to treat infection and prevent pneumocystis carinii pneumonia. [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]

**Tuberculosis:** Any of the infectious diseases of man and other animals caused by species of Mycobacterium. [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]

**Tympanic membrane:** A thin, tense membrane forming the greater part of the outer wall of the tympanic cavity and separating it from the external auditory meatus; it constitutes the boundary between the external and middle ear. [NIH]

**TYPHI:** The bacterium that gives rise to typhoid fever. [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]

**Ubiquitin:** A highly conserved 76 amino acid-protein found in all eukaryotic cells. [NIH]

**Ulcer:** A localized necrotic lesion of the skin or a mucous surface. [NIH]

**Ulceration:** 1. The formation or development of an ulcer. 2. An ulcer. [EU]

**Ulcerative colitis:** Chronic inflammation of the colon that produces ulcers in its lining. This condition is marked by abdominal pain, cramps, and loose discharges of pus, blood, and mucus from the bowel. [NIH]

**Unconscious:** Experience which was once conscious, but was subsequently rejected, as the "personal unconscious". [NIH]

**Uraemia:** 1. An excess in the blood of urea, creatinine, and other nitrogenous end products of protein and amino acids metabolism; more correctly referred to as azotemia. 2. In current usage the entire constellation of signs and symptoms of chronic renal failure, including nausea, vomiting anorexia, a metallic taste in the mouth, a uraemic odour of the breath, pruritus, uraemic frost on the skin, neuromuscular disorders, pain and twitching in the muscles, hypertension, edema, mental confusion, and acid-base and electrolyte imbalances. [EU]

**Ureters:** Tubes that carry urine from the kidneys to the bladder. [NIH]

**Urethra:** The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

**Urinary:** Having to do with urine or the organs of the body that produce and get rid of urine. [NIH]

**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]

**Urodynamics:** The mechanical laws of fluid dynamics as they apply to urine transport. [NIH]

**Urogenital:** Pertaining to the urinary and genital apparatus; genitourinary. [EU]

**Uterus:** The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the womb. [NIH]

**Vaccination:** Administration of vaccines to stimulate the host's immune response. This includes any preparation intended for active immunological prophylaxis. [NIH]

**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]

**Vacuoles:** Any spaces or cavities within a cell. They may function in digestion, storage, secretion, or excretion. [NIH]

**Vagina:** The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

**Vaginal:** Of or having to do with the vagina, the birth canal. [NIH]

**Vaginitis:** Inflammation of the vagina characterized by pain and a purulent discharge. [NIH]

**Vaginosis:** A condition caused by the overgrowth of anaerobic bacteria (e. g., Gardnerella vaginalis), resulting in vaginal irritation and discharge. [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]

**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]

**Vasodilators:** Any nerve or agent which induces dilatation of the blood vessels. [NIH]

**VE:** The total volume of gas either inspired or expired in one minute. [NIH]

**Vector:** Plasmid or other self-replicating DNA molecule that transfers DNA between cells in nature or in recombinant DNA technology. [NIH]

**Vegetative:** 1. Concerned with growth and with nutrition. 2. Functioning involuntarily or unconsciously, as the vegetative nervous system. 3. Resting; denoting the portion of a cell cycle during which the cell is not involved in replication. 4. Of, pertaining to, or characteristic of plants. [EU]

**Vein:** Vessel-carrying blood from various parts of the body to the heart. [NIH]

**Venereal:** Pertaining or related to or transmitted by sexual contact. [EU]

**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]

**Venous Thrombosis:** The formation or presence of a thrombus within a vein. [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]

**Ventricular Remodeling:** The geometric and structural changes that the ventricle undergoes, usually following myocardial infarction. It comprises expansion of the infarct and dilatation of the healthy ventricle segments. While most prevalent in the left ventricle, it can also occur in the right ventricle. [NIH]

**Venules:** The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

**Vertebrae:** A bony unit of the segmented spinal column. [NIH]

**Vertigo:** An illusion of movement; a sensation as if the external world were revolving around the patient (objective vertigo) or as if he himself were revolving in space (subjective vertigo). The term is sometimes erroneously used to mean any form of dizziness. [EU]

**Vestibule:** A small, oval, bony chamber of the labyrinth. The vestibule contains the utricle and saccule, organs which are part of the balancing apparatus of the ear. [NIH]

**Veterinary Medicine:** The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

**Villi:** The tiny, fingerlike projections on the surface of the small intestine. Villi help absorb nutrients. [NIH]

**Vinblastine:** An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. It is a mitotic inhibitor. [NIH]

**Vinca Alkaloids:** A class of alkaloids from the genus of apocyanaceous woody herbs including periwinkles. They are some of the most useful antineoplastic agents. [NIH]

**Vincristine:** An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

**Viomycin:** A strongly basic, antibiotic complex from several strains of Streptomyces. It is allergenic and toxic to kidneys and the labyrinth. Viomycin is used in tuberculosis as several different salts and in combination with other agents. [NIH]

**Viral:** Pertaining to, caused by, or of the nature of virus. [EU]

**Virulence:** The degree of pathogenicity within a group or species of microorganisms or viruses as indicated by case fatality rates and/or the ability of the organism to invade the tissues of the host. [NIH]

**Virus:** Submicroscopic organism that causes infectious disease. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

**Virus Diseases:** A general term for diseases produced by viruses. [NIH]

**Vitreous Hemorrhage:** Hemorrhage into the vitreous body. [NIH]

**Vitro:** Descriptive of an event or enzyme reaction under experimental investigation occurring outside a living organism. Parts of an organism or microorganism are used together with artificial substrates and/or conditions. [NIH]

**Vivo:** Outside of or removed from the body of a living organism. [NIH]

**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]

**Vulva:** The external female genital organs, including the clitoris, vaginal lips, and the opening to the vagina. [NIH]

**Vulvovaginitis:** Inflammation of the vulva and vagina, or of the vulvovaginal glands. [EU]

**War:** Hostile conflict between organized groups of people. [NIH]

**Warfarin:** An anticoagulant that acts by inhibiting the synthesis of vitamin K-dependent coagulation factors. Warfarin is indicated for the prophylaxis and/or treatment of venous thrombosis and its extension, pulmonary embolism, and atrial fibrillation with embolization. It is also used as an adjunct in the prophylaxis of systemic embolism after myocardial infarction. Warfarin is also used as a rodenticide. [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]

**Womb:** A hollow, thick-walled, muscular organ in which the impregnated ovum is developed into a child. [NIH]

**Wound Healing:** Restoration of integrity to traumatized tissue. [NIH]

**Wound Infection:** Invasion of the site of trauma by pathogenic microorganisms. [NIH]

**Wounds, Gunshot:** Disruption of structural continuity of the body as a result of the discharge of firearms. [NIH]

**Xenograft:** The cells of one species transplanted to another species. [NIH]

**X-ray:** High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [NIH]

**Yeasts:** A general term for single-celled rounded fungi that reproduce by budding. Brewers' and bakers' yeasts are Saccharomyces cerevisiae; therapeutic dried yeast is dried yeast. [NIH]

**Yolk Sac:** An embryonic membrane formed from endoderm and mesoderm. In reptiles and birds it incorporates the yolk into the digestive tract for nourishing the embryo. In placental mammals its nutritional function is vestigial; however, it is the source of most of the intestinal mucosa and the site of formation of the germ cells. It is sometimes called the

vitelline sac, which should not be confused with the vitelline membrane of the egg. [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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