EMPHYSEMA

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

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

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

Printed in the United States of America.

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

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

Publisher's note: The ideas, procedures, and suggestions contained in this book are not intended for the diagnosis or treatment of a health problem. As new medical or scientific information becomes available from academic and clinical research, recommended treatments and drug therapies may undergo changes. The authors, editors, and publisher have attempted to make the information in this book up to date and accurate in accord with accepted standards at the time of publication. The authors, editors, and publisher are not responsible for errors or omissions or for consequences from application of the book, and make no warranty, expressed or implied, in regard to the contents of this book. Any practice described in this book should be applied by the reader in accordance with professional standards of care used in regard to the unique circumstances that may apply in each situation. The reader is advised to always check product information (package inserts) for changes and new information regarding dosage and contraindications before prescribing any drug or pharmacological product. Caution is especially urged when using new or infrequently ordered drugs, herbal remedies, vitamins and supplements, alternative therapies, complementary therapies and medicines, and integrative medical treatments.

Cataloging-in-Publication Data

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

Emphysema: A Medical Dictionary, Bibliography, and Annotated Research Guide to Internet References / James N. Parker and Philip M. Parker, editors
p. cm.
Includes bibliographical references, glossary, and index.
ISBN: 0-597-84206-X
1. Emphysema-Popular works. I. Title.

Disclaimer

This publication is not intended to be used for the diagnosis or treatment of a health problem. It is sold with the understanding that the publisher, editors, and authors are not engaging in the rendering of medical, psychological, financial, legal, or other professional services.

References to any entity, product, service, or source of information that may be contained in this publication should not be considered an endorsement, either direct or implied, by the publisher, editors, or authors. ICON Group International, Inc., the editors, and the authors are not responsible for the content of any Web pages or publications referenced in this publication.

Copyright Notice

Acknowledgements

The collective knowledge generated from academic and applied research summarized in various references has been critical in the creation of this book which is best viewed as a comprehensive compilation and collection of information prepared by various official agencies which produce publications on emphysema. 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.

About the Editors

James N. Parker, M.D.

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

Philip M. Parker, Ph.D.

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

About ICON Health Publications

To discover more about ICON Health Publications, simply check with your preferred online booksellers, including Barnes&Noble.com and Amazon.com which currently carry all of our titles. Or, feel free to contact us directly for bulk purchases or institutional discounts:

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

Table of Contents

FORWARD

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

The Editors

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

CHAPTER 1. STUDIES ON EMPHYSEMA

Overview

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

The Combined Health Information Database

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

- **Surgical Emphysema and Pneumomediastinum Complicating Dental Extraction**

  Source: British Dental Journal. 188(11): 589-590. June 10, 2000.

  Contact: Available from Stockton Press. Houndmills, Basingstoke, Hampshire, RG21 6XS, United Kingdom. E-mail: subscriptions@nature.com.

  Summary: Subcutaneous and mediastinal emphysema is a rare complication of dental extraction and the use of air turbines has often been implicated. In this article, the authors describe a case which highlights a serious complication of the use of an air rotor for the removal of a right second mandibular molar. During this procedure, potential microbial contaminants such as pseudomonas and legionella in dental compressed air lines may be passed into tissue spaces. The authors conclude by recommending that the use of an air rotor during dental surgery be abandoned. 2 figures. 1 references.

Federally Funded Research on Emphysema

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

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

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

- **Project Title: 92 KDA GELATINASE AND COLLAGENASES IN EMPHYSEMA**

  Principal Investigator & Institution: Senior, Robert M.; Professor; Barnes-Jewish Hospital Ms 90-94-212 St. Louis, Mo 63110

  Timing: Fiscal Year 2001; Project Start 19-FEB-1992; Project End 31-JUL-2002

  Summary: Proteolytic activity that destroys lung elastic fibers is considered pivotal in the pathogenesis of pulmonary **emphysema,** a condition found primarily among smokers with chronic obstructive lung disease (COPD). Neutrophils and alveolar macrophages have been examined closely as possible sources for the elastase activity that causes **emphysema.** While some evidence suggests an important role for neutrophils, several observations point to alveolar macrophages as critical in the pathogenesis of **emphysema** in smokers: smokers' lungs have greatly increased (10 to 20 fold) numbers of macrophages, macrophages accumulate in smokers' lungs at precisely the sites of early **emphysema,** and macrophages are known to release a variety of proteinases that can attack components of the extracellular matrix. Furthermore, we have demonstrated that human alveolar macrophages cultured in contact with elastin have significant capacity to degrade this substrate via a mechanism which is near completely metalloproteinase-dependent. Despite these suggestive features, however, it has proven difficult to implicate human macrophages directly in the pathogenesis of **emphysema** because there has been limited evidence for a human macrophage enzyme with the capacity to degrade elastin. Recently, we discovered that one of the major proteinases released by human alveolar macrophages, a 92-kDa metalloproteinase, has pronounced elastolytic activity. This finding represents the first definitive demonstration of a neutral proteinase secreted by human macrophages that degrades elastin. To extend these initial observations we propose to examine in detail the elastolytic properties of the 92-kDa metalloproteinase, determine the role of this enzyme in the capacity of human alveolar macrophages to degrade elastin, look for evidence of excessive 92-kDa enzyme in human lung tissue affected with **emphysema,** and establish whether this human enzyme can produce pulmonary **emphysema** in experimental animals. These studies will use: (1) enzymologic techniques to define the binding

[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).

affinity of the 92-kDa enzyme for elastin, its catalytic parameters, and sites of substrate cleavage; (2) specific antiserum to the 92-kDa enzyme and the administration of antisense oligonucleotides to block endogenous 92-kDa enzyme and determine its role in macrophage-mediated elastolysis; (3) in situ hybridization to localize expression of 92-kDa mRNA in emphysematous human lung tissues, and; (4) histopathology to determine the effects of recombinant 92-kDa metalloproteinase on the lungs of experimental animals. These studies will contribute new ideas to our understanding of the pathogenesis of **emphysema** and will lead to new strategies for the prevention and control of **emphysema** and COPD.

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

- **Project Title: A TRANSCRIPTIONAL PROGRAM REGULATING MYELOPOIESIS**

  Principal Investigator & Institution: Friedman, Alan D.; Associate Professor; Oncology Center; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

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

  Summary: (Applicant's Description Verbatim): Myeloid cells are important in many disease processes, including leukemia, marrow failure, auto-immune diseases, and **emphysema.** C/EBPalpha (C/EBPa) and PU.1 are key regulators of myelopoiesis. C/EBPa null mice lack granulocytes, and PU.1 null mice lack B cells, granulocytes, and monocytes. 32D cl3 myeloid cells were developed expressing C/EBPa-ER or PU.1-ER. Activation of C/EBPa-ER increased MPO, lactoferrin, and G-CSF receptor mRNA expression and induced a neutrophilic morphology and a G1 cell cycle arrest. In contrast, activation of PU.1-ER only induced MPO RNA. PU.1 mRNA was rapidly induced by C/EBPa-ER, even in the presence of cycloheximide. Thus, the central hypothesis of aim1 is that C/EBPa activates the PU.1 gene in normal hematopoietic cells. Cis elements in the PU.1 gene which mediate this activation will be identified. The effect of retroviral expression of C/EBPa-ER in C/EBPa-null cells and of transgenic expression of C/EBPa in B cells on PU.1 levels will be determined. Aim 2 will test the hypothesis that PU.1 is not as effective as C/EBPa for induction of myeloid genes in normal cells. PU.1 will be expressed in C/EBPa-null cells using a retroviral vector and in B cells using the Ig u enhancer. The effect of PU.1 on myeloid genes and on C/EBPa expression will be assessed. Other C/EBPs may compensate for the lack of C/EBPa in C/EBPa null mice. 32D cl3 lines were characterized expressing KRAB-C/EBPa-ER, containing the C/EBPa DNA-binding domain and the KRAB repression domain. Activation of this protein potently inhibits global C/EBP activities, and consequently G-CSF receptor RNA expression is reduced. 32D cl3 cells expressing activated KRAB-C/EBPa-ER and exogenous G-CSF receptor do not differentiate to neutrophils or express MPO RNA, but develop an immature, monocytic morphology. If C/EBP inhibition is relieved after 24 hrs, the cells no longer can mature to neutrophils. Aims 3 will test the hypotheses that C/EBPs are required for both monopoiesis and granulopoiesis, but that a modest decrease in C/EBP activities is permissive for monopoiesis if exogenous M-CSF receptor is provided. KRAB-C/EBPa-ER will be expressed in 32D cl3 cells or in normal hematopoietic cells, as a transgene or using retroviral vectors, alone, with the G-CSF receptor, or with the M-CSF receptor. Myelopoiesis at various levels of C/EBP activity and progenitor fate after various times of C/EBP inhibition will be assessed.

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

- **Project Title: ADENOVIRAL INFECTION IN THE PATHOGENESIS OF EMPHYSEMA**

  Principal Investigator & Institution: Hogg, James C.; Professor of Pathology; University of British Columbia 2075 Wesbrook Pl Vancouver,

  Timing: Fiscal Year 2001; Project Start 29-SEP-2000; Project End 31-AUG-2004

  Summary: (adapted from the applicants' abstract) Cigarette smoking is the major risk factor for the development of **emphysema** but only a relatively small proportion of cigarette smokers develop this complication. The investigators' work suggests that latent adenoviral infection of the lung adds risk by amplifying cigarette smoke induced inflammation to a level capable of causing emphysematous lung destruction. The investigators propose to test this hypothesis on surgically resected human lung specimens and on cultured cells derived from this tissue. The investigators' first goal is to compare normal regions of the lung, to regions with mild and severe **emphysema** using laser capture microdissection and micro assay technologies to determine if increased adenoviral DNA results in increased inflammatory gene expression in **emphysema.** The second group of experiments will determine if cytokines generated from alveolar macrophages obtained from these lungs stimulate adenoviral E1A transfected lung epithelial cells to generate excess inflammatory mediators in vitro. A third group of studies will examine the nature of the migration of neutrophils through the alveolar wall in cigarette smoke induced inflammation to determine the nature and effect of the contact between the polymorphonuclear cell and the alveolar wall elastin network. The fourth set of studies will focus on the nature of adenoviral DNA integration into the host respiratory epithelial cell genome to determine if the site of integration effects the production of inflammatory mediators. Finally, the investigators will determine the genetic susceptibility to latent adenoviral integration in the human lung. The information gathered from these studies will provide new insights into the pathogenesis of **emphysema** and help explain why some smokers develop **emphysema** and others do not.

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

- **Project Title: AEROSOLIZED HYALURONIC ACID AS A TREATMENT FOR EMPHYSEMA**

  Principal Investigator & Institution: Cantor, Jerome O.; Exhale Therapeutics, Inc. 1301 Shoreway Rd, Ste 320 Belmont, Ca 940024106

  Timing: Fiscal Year 2001; Project Start 10-SEP-2001; Project End 31-AUG-2003

  Summary: (provided by applicant): Chronic obstructive pulmonary disease afflicts 12-14 million people in the US and in an advanced form, **emphysema,** disables 2 million and ultimately leads to death. No approved, existing treatment can arrest emphysema's progressive destruction of the lung. Exhale Therapeutics, Inc intends to develop and commercialize aerosolized hyaluronic acid (HA) into the first effective therapeutic product that can preserve lung function. The long-term objectives of the proposed project (Phases I) are: (1) to show that aerosolized low-molecular weight HA inhaled daily protects against lung elastic fiber injury and subsequent destruction of alveoli; and (2) to elucidate the protective mechanism. The specific aim of Phase I is to demonstrate that in mice exposed regularly to tobacco smoke in a chamber that simulates cigarette smoking, daily treatment with HA administered as an aerosol significantly reduces the severity of emphysematous damage to their lungs. Two groups of mice will smoke, the first will receive daily treatment with HA dissolved in distilled water, and the second will receive nebulized water only. A comparison of the mean linear intercept of lung

sections of the two groups will provide a direct quantitative measure of the protective effect of HA. Other semi-quantitative measures will provide supporting evidence. PROPOSED COMMERCIAL APPLICATION: Hyaluronic acid (HA) has the potential to become an effective therapeutic agent that can protect lung function against the chronic destruction of alveoli in **emphysema.** Since no treatment for pulmonary **emphysema** currently exists, proof of safety and efficacy in humans will permit rapid commercialization. The proposed research in an animal model will accelerate the formulation of a therapeutic product for study and use in humans.

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

- **Project Title: ALVEOLIZATION IN FIBRILLIN-1 DEFECTIVE MICE**

  Principal Investigator & Institution: Neptune, Enid R.; Assistant Professor; Medicine; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2001; Project Start 13-AUG-2001; Project End 31-JUL-2006

  Summary: (provided by applicant): Diseases of impaired gas exchange, such as **emphysema** and lung fibrosis, are prevalent, clinically burdensome ,and difficult to treat. Because lung transplantation remains the only definitive treatment option for these diseases, much interest has been focused upon understanding the cellular and molecular basis of alveolar formation. As the current knowledge of mammalian lung alveolization is quite limited, this grant is directed towards exploring the mechanism of impaired alveolar septation in mouse models in an effort to understand the requirements of normal septation. The PI has recently observed distal airspace enlargement in two strains of fibrillin-I deficient mice and has found that TGF-beta is a critical mediator of this defect. The first objective is to determine the natural history of impaired septation in three fibrillin-1 defective mouse models. This pursuit should establish whether septation defects may represent important risk factors for the development of **emphysema** and pulmonary fibrosis. The natural history of the alveolization defects in these models will be correlated with the evolution of aberrant TGF-beta signaling previously observed in two of the models. The second objective is to identify the pulmonary morphologic aberrations which precede the observed septation defects in an effort to reveal critical mediators of septation. Several approaches will be employed to establish whether abnormalities in pulmonary vascular development, matrix composition, or both underlie the disruptions in septation. The final objective is to use chip-based gene expression profiling of murine lung to identify novel and important mediators of septation. The PI of this project is an instructor in the Department of Medicine. She is committed to a career in academic medicine and plans to spend 80 percent of her time in research pursuits. She has had previous training in signal transduction and, more recently, the use of transgenic mouse models to probe human disease. She now wants to expand her research interests to investigating mammalian lung development. To achieve this, she will take sponsored courses on murine development and attend lectures in the developmental genetics department at Johns Hopkins School of Medicine. The environment at Johns Hopkins provides several esteemed scientists who can provide guidance in the use of mouse models to probe lung pathology and developmental aberrations. Their involvement as well as a formal education program in both the Division of Pulmonary Medicine and Institute of Genetic Medicine should facilitate the achievement of her stated research objectives as well as aid in her development into a fully independent investigator.

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

- **Project Title: ANALYSIS OF THE AIRWAY ANTIPROTEINASE DEFENSE SYSTEM**

  Principal Investigator & Institution: Cataltepe, Sule U.; Children's Hospital (Boston) Boston, Ma 021155737

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

  Summary: (Adapted from applicant's abstract) Proteinases play a major role in the development of inflammatory lung diseases such as cystic fibrosis, asthma, chronic bronchitis, **emphysema** and chronic lung disease of prematurity. A better understanding of the regulation of proteinases by inhibitors synthesized by the lung itself could facilitate efforts to develop specific treatments for these diseases. Squamous cell carcinoma antigens (SCCA) 1 and 2 are members of the high molecular weight serine proteinase inhibitor (serpin) family. Although SCCA1 inhibits lysosomal cysteine proteinases, cathepsins (cat)L,S and K, whereas SCCA2 inhibits chymotrypsin-like serine proteinases, catG and mast cell chymase. SCCA1 and SCCA2 show a tissue restricted expression pattern and are co-localized in the tracheal, bronchial and bronchiolar epithelium. In addition, target proteinases of SCCA1, catS and catK, are expressed by the airway epithelial cells. Another source of these potent elastolytic cysteine proteinases in the lung is alveolar macrophages. Based on the in vitro inhibitory profiles and distribution patterns of SCCA1 and SCCA2 in the airways, the investigators hypothesize that these two serpins protect the airways against proteinase mediated injury. The objective of this proposal is to test this hypothesis using in vitro cell culture and in vivo transgenic animal models. The specific aims of the proposed project are to: 1) characterize the deleterious effects of exogenous and endogenous cysteine proteinases catS and catK on bronchial epithelial cells in vitro, 2) determine whether SCCA1 and/or SCCA2 can protect cultured bronchial epithelial cells from the proteinase-mediated injury and isolate the target proteinases, 3) determine whether targeted expression of SCCA1 and SCCA2 can protect the airways from proteinase-mediated injury. The experimental design involves use of cell cultures in conjunction with stable transfections to overexpress SCCA1 and SCCA2. Barrier function of the airway epithelium will be studied by permeability and transepithelial resistance measurements as well as structural analysis. Affinity chromatography and co-immunoprecipation will be used to identify the target proteinases of SCCA1 and SCCA2 in proteinase-mediated injury in vivo. The rat clara cell 10kD protein promoter (CC10) will be used to target expression of SCCA1 and SCCA2 genes to the lung. Animals will be examined to determine the extent of protection against proteinase-mediated lung injury following exposure to acrolein. These studies should enhance our understanding of the mechanisms of proteinase mediated injury and whether the locally synthesized inhibitors such as SCCA1 and SCCA2 can prevent this type of damage.

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

- **Project Title: APPLIED GENOMICS IN CARDIOPULMONARY DISEASE**

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

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-JUL-2004

  Summary: The overall goal of the Animal/Proteomic Component of the "Applied Genomic Program in Cardiopulmonary Disease" is to define and test the relevance of disease specific gene candidates that predict lung and cardiac remodeling in animal models of cardiopulmonary diseases utilizing gene profiling approaches. Identification of susceptibility genes for human disease is hampered by variability in clinical phenotype, genetic heterogeneity in human populations and the experimental difficulty

in addressing the molecular mechanisms underlying complex pathological processes in humans. Thus our strategy is to take advantage of the experimental tractability of murine models of disease to provide high quality of candidate genes underlying remodeling processes in multiple cardiopulmonary disease. To achieve this goal, we have assembled an outstanding group of investigators with broad and overlapping expertise with animal models of cardiopulmonary diseases including asthma, pulmonary fibrosis, cardiac failure, **emphysema,** hyperoxia-induced lung injury and pulmonary hypertension. Our preliminary data suggest that these models are predictive of human disease and that the gene profiling approach can successfully be used to identify genes important in human disease. The specific aims of this component are l) to define a set of predictor genes for tissue remodeling using Affymetrix 5000 predictor oligonucleotide microarrays (Mu19K) in each of the six animal models of disease; 2) to refine the number of candidate genes and to establish the kinetics of gene expression by constructing custom cDNA arrays for 1000-5000 predictor genes in each model; and 3) to compare and contract gene expression profiles between models and human systems in order to prioritize candidates for further analysis by proteomic and single nucleotide polymorphism (SNPs) approaches; 4) to utilize proteomic approaches to study the consequences of changes in gene expression at the cell and tissue level; and 5) to being to determine the functional relevance of this focused set of genes to remodeling processes by utilizing transgenic and knockout technologies. The combined (mouse and human) approach of this program to the identification of disease specific genes for lung and cardiac remodeling should greatly facilitate future disease discovery.

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

- **Project Title: ASSESSING THE OCCUPATION BURDEN IN COPD**

  Principal Investigator & Institution: Blanc, Paul D.; Professor of Medicine; Medicine; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

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

  Summary: (From applicant's abstract): The aims are to assess the population burden of occupational exposures in the prevalence of chronic obstructive pulmonary disease (COPD) and to estimate the impact of selected occupational risks on the severity of progression of COPD. COPD is common and costly. The contribution of occupational risk factors to its prevalence and progression have not been well characterized. Better delineation of these associations has been identified as a priority area for study in the NIOSH National Occupational Research Agenda. A population sample of the continental United States of those aged 55-75, supplemented by an enriched sample in geographic "hot spots" identified by NIOSH through respiratory diseases mapping, will yield 2120 subjects, of whom 400 will have COPD defined by report of chronic bronchitis or **emphysema** without asthma. Structured telephone interviews will assess demographics, health status, smoking exposures, and occupational histories. High risk jobs will later be coded using a job matrix system independent of subject report of specific exposures. Two hundred of those with COPD, with over-sampling of those with greater severity, will be followed at 12-14 months to assess health status and health services utilization, as well as decrements in quality of life. This study will provide statistically powerful estimates of the occupational association with COPD. We should be able to identify a work-related RR of 1.35 which, coupled with an exposure frequency of 20 percent, would reflect a PAR percent of 6.5 percent. In the longitudinal study component, we should be able to detect a RR>2.1 for selected occupational risk factors as predictors of outcomes occurring in at least 10 percent of the group.

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

- **Project Title: BIOMARKERS IN SPUTUM IN COPD**

  Principal Investigator & Institution: Broide, David H.; Professor of Medicine; Medicine; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, Ca 92093

  Timing: Fiscal Year 2002; Project Start 23-SEP-2002; Project End 31-JUL-2006

  Summary: (provided by applicant): The overall goal of this proposal is to identify biomarkers in the sputum of patients with **emphysema** that associate with **emphysema** but not with either healthy controls, smokers without **emphysema,** or lung diseases associated with airway inflammation and fibrosis such as asthma or idiopathic pulmonary fibrosis. The approach we plan to use to identify sputum biomarkers in **emphysema** will use both hypothesis driven experiments to explore candidate sputum biomarkers of inflammation (LTB4, IL-8, TNF), fibrosis (TGF- beta, PGDF, FGF), metalloproteases (MMP-1, MMP-9, MMP-12, TIMP), elastin degradation (desmosine in urine) as well as an alternative approach using both proteomic analysis of sputum and bronchoalveolar lavage, and genomic studies of airway epithelium and alveolar macrophages to identify potential novel biomarkers of **emphysema** that correlate with CT scan evidence of **emphysema.** Levels of biomarkers will be measured over a two year period and be correlated with CT scan extent of **emphysema.** If such a non-invasive biomarker were identified this could either serve as a biomarker in studying the effects of intervention with anti-inflammatory medications or smoking cessation in subjects with **emphysema,** or alternatively serve to identify smokers at risk for the development of **emphysema.**

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

- **Project Title: BIOMARKERS OF OXIDATIVE STRESS AND INFLAMMATION IN COPD**

  Principal Investigator & Institution: Macnee, William; University of Edinburgh Edinburgh Eh8 9Yl, Scotland Edinburgh,

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

  Summary: (provided by applicant): Chronic Obstructive Pulmonary Disease (COPD) is a disease with a major unmet medical need, for which at present there is no effective treatment that will halt the decline in lung function. Development of new therapies is hampered by the lack of well defined clinical biomarkers to both characterize patients and assess drug efficacy. Oxidative stress and the associated inflammatory responses in the lungs are key elements in the pathogenesis of COPD. However, there have been no longitudinal studies to assess the utility of representative markers of oxidative stress and inflammation as biomarkers of disease severity and hence their potential as surrogate endpoints for assessment of the effectiveness of new therapeutic agents. The purpose of this project is to identify and characterize candidate markers of oxidative stress and inflammation in both cross sectional and longitudinal studies. The proposed biomarkers for these studies are the lipid peroxidation products 4-hydroxy-2-nonenal, F2alpha-isoprostanes, and cytokines such as interleukin (IL) IL-8, IL-6, IL-1, tumor necrosis factor-alpha (TNF-alpha) and vascular endothelial growth factor in a well characterized cohort of COPD patients in both cross sectional and longitudinal studies. A further aim is to relate the levels of these markers of oxidative stress to inflammatory mediators and differential cell counts in induced sputum. In addition, a population of COPD patients will be characterized according to the levels of surrogate markers of airway inflammation and oxidative stress, which will be related to disease severity and to the clinical phenotype of COPD. Sophisticated techniques such gas chromatography/mass spectrometry (GC/MS) will be used to measure specific and

stable lipid peroxidation products in peripheral blood, induced sputum and exhaled breath condensate. Moreover, mindful of the possibility that no single molecule will be a biomarker which is applicable to all patients with COPD, metabonomic and genomic technologies will be exploited to assess a spectrum of potential biomarkers, thus generating a 'finger print' characteristic of the disease. Such information will allow the identification of novel biomarkers and the fingerprints themselves may represent a mechanism to stratify COPD patients and allow the assessment of novel therapies.

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

- **Project Title: CATALYSIS OF THIOL DISULFIDE EXCHANGE**

  Principal Investigator & Institution: Gilbert, Hiram F.; Professor; Biochem and Molecular Biology; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2001; Project Start 01-JUL-1988; Project End 31-AUG-2003

  Summary: Proteins must fold into a correct conformation to attain biological function. In the cell, protein folding is assisted by catalysts that accelerate folding and by chaperones that inhibit aggregation. Protein misfolding and aggregation is a primary contributor to Alzheimer's disease, prion-mediated infection, **emphysema,** and cystic fibrosis. Misfolding also limits the use of recombinant proteins for therapeutic needs. Our long-term approach to these problems is to understand and mimic the behavior of cellular folding assistants in promoting correct folding. This proposal focuses on protein disulfide isomerase (PDI), a folding catalyst and a chaperone. PDI accelerates folding by catalyzing disulfide bond formation and rearrangement. As a chaperone, it inhibits substrate aggregation, but under certain conditions, PDI can facilitate aggregation. The immediate goals are to define the mechanisms for catalysis and to determine how PDI inhibits or stimulates aggregation. Specific Aim 1. The hypothesis to be tested is that PDI catalyzes disulfide isomerization by multiple cycles of reduction and oxidation. Mutagenesis will be used to inactivate alternative pathways for isomerization in vitro and in S. cerevisiae to examine the contributions of specific pathways. Specific Aim 2. The hypothesis is that PDI distinguishes between misfolded and native proteins by their stability. If correct, the hypothesis suggests that the ability of PDI to unfold its substrates should correlate with their stability. Specific Aim 3. The catalytic effectiveness of PDI can be attributed to an intermediate redox potential of the active site and/or the arrangement of PDI into structural domains. Mutagenesis will be used to alter the redox potential of PDI active sites to test its contribution to catalysis. The catalytic properties of deletion mutants will define the contribution of accessory domains. Specific Aim 4. A working model suggests that PDI facilitates aggregation by cross- linking smaller substrate aggregates through covalent and non- covalent interactions. Sedimentation velocity experiments will identify the species that aggregate. PDI mutants missing one or more structural domains will be studied to localize the sites of substrate interaction. The completion of these goals will suggest new strategies to encourage proper folding and to discourage aggregation.

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

- **Project Title: CHRONIC OBSTRUCTIVE PULMONARY DISEASE GENE LOCALIZATION**

  Principal Investigator & Institution: Hasstedt, Sandra J.; Associate Professor; Human Genetics; University of Utah 200 S University St Salt Lake City, Ut 84112

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

Summary: (Applicant's Abstract): Chronic obstructive pulmonary disease (COPD) is a slowly progressive disorder characterized by airways obstruction that lasts for at least several months. The two major causes of COPD are chronic bronchitis and **emphysema.** Either disorder may occur with or without airways obstruction, but airways obstruction causes impairment of lung function leading to disability and death. COPD is a major health problem in the United States and throughout the world, consistently ranking among the most common causes of death in the United States. Cigarette smoking is the primary environmental factor that increases the risk of COPD, but other environmental factors have also been implicated. However, despite a well-established role, environmental factors alone do not cause COPD. Symptomatic COPD develops in only 10-20 percent of heavy cigarette smokers, probably those with a genetic susceptibility, although common COPD susceptibility genes have yet to be identified. This project proposes a single specific aim: to localize, within the genome, a COPD susceptibility gene. The strategy proposed is to apply statistical linkage analysis to family data. Pulmonary measurements have already been collected on 159 members of 16 pedigrees and evidence supporting a COPD susceptibility gene in these pedigrees has been obtained from segregation analysis. Each of 11,995 genetic markers, which have already been genotyped on pedigree members, will be tested for evidence of linkage to the inferred COPD susceptibility gene. Evidence of linkage to one or more genetic markers will identify genomic locations of COPD susceptibility genes. The high density of markers will allow fine-mapping of the gene. Successful completion of this gene localization project is the necessary prerequisite for a project to identify and characterize a COPD susceptibility gene. Identifying a gene that when mutated increases the risk of COPD may increase understanding of pulmonary function, as well as allowing gene-carriers to be identified and made aware of their susceptibility.

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

- **Project Title: COGNITIVE EFFECTS OF LUNG VOLUME REDUCTION SURGERY**

  Principal Investigator & Institution: Kozora, Elizabeth; National Jewish Medical & Res Ctr and Research Center Denver, Co 80206

  Timing: Fiscal Year 2001; Project Start 01-FEB-2000; Project End 31-JAN-2003

  Summary: The primary goal of this study is to examine the neuropsychological functioning of **emphysema** patients undergoing lung volume reduction surgery (MT+LVRS) compared to medical therapy alone (MT). The study will include patients at two clinical sites for the National **Emphysema** Treatment Trial (NETT). Enhancements of ventilation and functional capacity are expected to contribute to greater long-term improvements in utilization of oxygen in the brain, thereby leading to improvements in cognitive performance greater than those observed among patients who exercise but do not receive LVRS (Specific Aim 1). A health control group will be retested on similar neuropsychological tests in order to control for practice effects (Specific Aim 2). Although we do not expect significant differences in emotional (depression and anxiety) functioning across groups, this study will enable us to evaluate the relationship between emotional status and neuropsychological scores in the MT+ LVRS and MT groups following randomization. In addition, since major neurological events are more likely following surgery, and major neurological events affect cognitive function, we will evaluate the incidence of neurological events in our sample and will determine the degree to which neurological events are associated with cognitive function (Specific Aim 3). No studies have examined the relationship between change in cognition and improve quality of life in COPD patients following LVRS surgery, therefore, we aim to explore these associations in Specific Aim 4. We propose to compare changes following LVRS

and MT by examining 84 NETT patients (42 in MT, 42 in LVRS) at three times points (baseline, post 6-10 week medical treatment MT, and 6 months post MT or LVRS randomization) using select neuropsychological, psychological, neurological and QoL tests. Forty normal controls will be tested at baseline and 6-10 weeks follow- up.

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

- **Project Title: CONTROL OF PULMONARY ELASTOLYTIC INJURY BY PROTEOGLYCANS**

  Principal Investigator & Institution: Nugent, Matthew A.; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 02118

  Timing: Fiscal Year 2002; Project Start 20-DEC-2001; Project End 30-NOV-2006

  Summary: An imbalance in protease/anti-protease activity is believed to underlie the development of obstructive pulmonary diseases such as **emphysema.** While elastin degradation is pivotal to this process it is clear that there are other targets of the excessive proteolysis that are involved in regulating the structural integrity of the alveolar wall. Our studies have demonstrated that pulmonary proteoglycans are a major target for elastase degradation. We have demonstrated that heparan sulfate proteoglycans in the extracellular matrix of pulmonary fibroblast are sites of storage for FGF2, a potent down regulator of elastin gene transcription. Within this project we aim to identify the functions and underlying mechanisms of proteoglycans as modulators of elastolytic injury in the lung. Our hypothesis is that elastase-induced lung injury results in the release of proteoglycans, growth factors and cytokines which mediate subsequent matrix repair. In the present project we will focus on the function of released proteoglycans as mediators of growth factor and elastase activity, the synthesis of proteoglycans after injury regulated by cytokines, and the relationship between proteoglycans and elastogenesis. The specific aims of this project are to: 1) Identify the role of elastase released heparan sulfate proteoglycans in modulating elastase activity, FGF2 receptor activation, and the synthesis of proteoglycans and elastin, 2) Define the role of the small chondroitan sulfate proteoglycan, decorin, in modulating the elastase-induced cellular response, 3) Determine the consequences of elastase digestion on FGF2 nuclear localization and on FGF2 and TGFbeta transport through extracellular matrix, and 4) Examine the effects of elastolytic injury on proteoglycan and growth factor levels in normal mice and mice deficient in IL-1beta and TNFalpha receptors, and decorin. These studies will help identify aspects of the lung response to injury that are mediated by proteoglycans. Ultimately, these studies could provide critical insight into the development of new treatments for obstructive pulmonary diseases targeting the regulatory role of proteoglycans.

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

- **Project Title: COPD CLINICAL RESEARCH NETWORK - DATA COORDINATING CENT***

  Principal Investigator & Institution: Connett, John E.; Professor; Biostatistics; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

  Timing: Fiscal Year 2003; Project Start 15-SEP-2003; Project End 31-JUL-2008

  Summary: (provided by applicant): The Division of Biostatistics in the School of Public Health at the University of Minnesota (John Connett, PI), in collaboration with the Divisions of Epidemiology and Pulmonary Medicine, proposes to establish and operate the Data Coordinating Center (DCC) for the Chronic Obstructive Pulmonary Disease Clinical Research Network. The goals of the Network are to identify preventive and

therapeutic interventions to reduce mortality, exacerbations, and disability in patients with moderate-to-severe COPD. Clinical trials undertaken by the Network must have relevance to clinical practice for the treatment of this common and serious chronic disease, and must provide efficient answers to questions regarding treatment alternatives. As described in RFA HL-03-002, four-to-six clinical centers and the DCC will launch and complete 4-5 clinical trials in a 5-year period, with 2-3 protocols in operation simultaneously. As the DCC for the Network we will perform the following key functions: 1) establish the Network's organizational structure and facilitate internal communications; 2) provide statistical input on study design; 3) develop and maintain Manuals of Procedures; 4) establish a distributed data entry/data management system; 5) train and certify clinical center personnel; 6) create subcontracts with central laboratories and reading centers, as needed; 7) generate randomization schedules and reports to monitor data quality, recruitment progress, retention, outcomes, and adverse events; 8) carry out data analyses for the investigators and contribute to manuscripts and scientific presentations. Our group brings to this project over 16 years of experience in the design, conduct, and analysis of multicenter clinical trials of COPD and **emphysema,** including the Lung Health Studies I, II, and the Feasibility of Retinoid Therapy for **Emphysema** (FORTE) study. We have assembled a solid and productive team of investigators and professional staff with relevant expertise in biostatistics, clinical trials, epidemiology, and pulmonary medicine, and ample experience in data management, data quality control, and statistical analysis.

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

- **Project Title: CORE-- RESPIRATORY DISORDERS RESEARCH FACILITY**

  Principal Investigator & Institution: Rothman, Paul B.; Professor; Columbia Univ New York Morningside 1210 Amsterdam Ave, Mc 2205 New York, Ny 10027

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

  Summary: The goals of the NIEHS Respiratory Disorders Research Core are to: 1) facilitate epidemiological research on causation of respiratory diseases among the population of northern Manhattan; 2) serve as a resource for interdisciplinary studies which utilize the diverse expertise of core members to study the mechanisms underlying respiratory diseases; and 3) facilitate cross fertilization of ideas and approaches to study respiratory diseases. The Center formalizes these interactions and provides resources for these interactive projects.

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

- **Project Title: CORE--ENVIRONMENTAL LUNG DISEASE**

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

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

  Description (provided by applicant): The overall objectives of this Research Core are to develop and promote new understandings of the effects of urban air pollution on the human body. This goal will be implemented by pilot research projects, interactive research seminars, and pre/postdoctoral student training. Specific research activities in Research Core 4 fall within the first four of the general Research Core elements listed above, but within each broad element, there are individual specific aims. These include: 1) Determination of the movement of soluble and insoluble particles after deposition in the lung; 2) Determination of the molecular genetic and inflammatory environment of exposed respiratory tissues and cells; 3) Evaluation of the pathophysiologic mechanisms

associated with the effects of these inhalants on pulmonary tissues and cellular responses; and 4) Interpretation of these relations in terms of health risks from human exposures; a major focus within elements 2 and 3 in the past has been a better understanding of the mechanism of hyperreactive airways and obstructive airway diseases, with special emphasis on asthma. How environmental pollutants affect the epithelium and airway smooth muscles has direct relevance to the response of asthmatics breathing in polluted air. In the inner cities such air pollution can lead to a condition known as urban asthma. This research, along with that in the first Core element, will form the scientific basis for new and increasing outreach focus involving the human exposure assessment research in Research Core 1. The Johns Hopkins Center for Childhood Asthma in the Urban Environment, headed by Dr. Eggleston, also may provide opportunity for new mechanistic understandings related to this human pathology. Risks for **emphysema** and lung cancer are also high in inner cities, and new projects in the Core with collaboration with Research Core 3 will begin to look at underlying mechanisms of these pathologies. Finally an increasingly important direction that will be expanded is the interaction of air pollution with viral infections. Two new faculty members (Jacoby and Imani) to the Core with immunologic expertise will lead this effort. A long range Research Core aim is to be able to investigate this spectrum of questions related to a variety of urban airborne pollutants, from the quantitative analysis of the exposure magnitude to a quantitative understanding of basic pathophysiologic responses of cells and tissues to these exposures. At the present time this global approach within the Research Core is fairly well developed for ozone, particulate matter, and viral infections, with studies spanning the spectrum from molecular genetics to human exposures. It is important to emphasize that the members of this Core are physiologists, pharmacologists, immunologists, pathologists, and pulmonary physicians who investigate basic mechanisms underlying environmental insults to the lung. As noted above, the investigators feel that this multi-disciplinary background is a major strength of this Research Core, providing the NIEHS Center with a unique perspective on environmental studies.

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

- **Project Title: CORE--MORPHOLOGY**

  Principal Investigator & Institution: Wert, Susan E.; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

  Timing: Fiscal Year 2001; Project Start 01-SEP-1996; Project End 31-JUL-2006

  Summary: (Applicant's Abstract) The Morphology Core will provide technical expertise, assistance and equipment to those investigators who wish to analyze their experiments using microscopic and morphometric techniques. Expertise and assistance will be provided by core personnel in the following areas: (1) routine light microscopy and histochemical analysis, (2) enzyme histochemistry, (3) immunohistochemistry, (4) in situ hybridization histochemistry, (5) autoradiography, (6) photomicroscopy, (7) electron microscopy, (8) confocal microscopy, (9) computer-assisted image analysis, and (10) morphometry. In addition, the Morphology Core will facilitate the acquisition, processing and storage of experimental and control tissues; maintain standards and quality control for histochemical procedures; and assist in the development of new techniques as needed. The Morphology Core will also be responsible for immunohistochemical and in situ hybridization analyses of human biopsy and autopsy material related to neonatal respiratory distress syndrome pulmonary alveolar proteinosis, hyaline membrane disease, bronchopulmonary dysplasia, interstitial lung disease, **emphysema,** and pulmonary malformations. The overall goal of these clinical

studies will be to characterize and identify mechanisms that cause idiopathic lung disease and developmental abnormalities.

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

- **Project Title: CYTOLYTIC ATTACK AGAINST LUNG PARENCHYMA IN EMPHYSEMA**

  Principal Investigator & Institution: Knoell, Daren L.; Associate Professor; None; Ohio State University 1800 Cannon Dr, Rm 1210 Columbus, Oh 43210

  Timing: Fiscal Year 2002; Project Start 01-JAN-2002; Project End 30-NOV-2006

  Summary: (provided by applicant): Many asymptomatic HIV-infected individuals develop alveolitis followed by **emphysema** but the pathogenesis remains unknown. We have found that cytotoxic lymphocytes (CTLs) are elevated in the airway of subjects that develop **emphysema** and that these patients have substantial morphologic evidence of parenchymal tissue loss. This corroborates other studies demonstrating that CTL elevation coincides with an early decline in diffusion capacity and an increase in lower airway epithelial permeability. A key observation is that CTLs isolated from the lung of HIV-infected subjects can accomplish MHC class 1 restricted killing of HIV infected cells. The focus of this investigation is to expand on a series of ground-breaking discoveries made by the applicant that reveal the following, 1) 141V infects human lung epithelial cells in vivo and in vitro; 2) the lung epithelium is permissive to HIV replication; and 3) that HIV infection of lung epithelial cells induces CTL-mediated apoptosis in an MHC restricted manner. Specific Aim 1 will test the hypothesis that primary human lung epithelial cells are infected by HIV-1 from the apical and basolateral surface and permit viral replication following cell (NF-0) activation. We predict that this will result in the release of competent free virus. Specific Aim 2 will test the hypothesis that HIV infection of primary human lung epithelial cells triggers a CTL-mediated assault resulting in epithelial cell apoptosis. In this pursuit we will identify the mechanism by which epithelial cell apoptosis occurs and then determine if a potent epithelial cell mitogen, keratinocyte growth factor, can prevent lung epithelial cell death. In the revised application we will develop a physiologically relevant model for studies with HIV. In particular, primary human lung epithelial cells will be grown on collagen coated trans-well inserts to establish fully differentiated monolayers with tight junctions at an air-liquid interface. The model will be used to identify preferential HIV transport which we believe is highly relevant since the epithelium may serve as a portal for HIV entry into the lung (basolateral to apical) as well as reintroduce virus back into the circulation (apical to basolateral). Subsequent studies will utilize the same model to identify how autologous, HIV-specific, CTLs dispose of the HIV+ lung epithelial cell. The long-term goal of the applicant is to establish a career in translational research that connects his current expertise in clinical medicine with basic science. The candidate has made a substantial commitment to pursue a career that will explore the lung parenchymal response to inflammation and translate discoveries into useful solutions for patients with lung disease. The applicant has established an excellent group of advisors to assist in this endeavor and has secured the appropriate institutional support to complete the training.

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

- **Project Title: DOSE RESPONSE MODELING IN EPIDEMIOLOGIC COHORT STUDIES**

  Principal Investigator & Institution: Eisen, Ellen A.; Environmental Health; Harvard University (Sch of Public Hlth) Public Health Campus Boston, Ma 02460

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

Summary: This proposal addresses the problem of nonlinear dose response estimation in environmental and occupational cohort studies by exploring two more flexible regression strategies: Generalized Additive Models (non-parametric regression) and a nonlinear dose metric. Typically, dose response models assume that the relationship is linear on some scale. Many disease mechanisms, however, such as sensitization or carcinogenesis, may produce nonlinearities in the dose-response curve. Moreover, linear models may be inappropriate in occupational cohort studies where the healthy worker effect can lead to an apparent plateau or even downturn in risk among the more highly exposed. General additive models will be used to describe the shapes of the dose-response curve between cumulative exposures and selected outcomes in three cohort mortality studies with well established exposure response associations. The three data sets available for dose-response modeling are: 46,400 autoworkers exposed to metalworking fluids, 5,414 Vermont granite workers exposed to silica in quartz form and 2,342 diatomaceous earth miners exposed to crystalline silica in cristobalite form. Disease outcomes of interest will include cancers of the stomach, esophagus, pancreas, and liver in the metalworking fluid cohort, and cancer of the lung in the two silica cohorts. Nonmalignant respiratory disease mortality will be examined in all cohorts. In addition, we will apply a flexible dose model for metalworking fluids and crystalline silica that includes simple cumulative exposure as a special case. Unlike standard analyses that are limited to linear relations with cumulative exposure, this model, proposed by Seixas, is sufficiently flexible to enable investigation of nonlinear dose-rate effects and variable disease induction/latency intervals. Secondary objectives include the direct comparisons of the carcinogenicity of the four types of metalworking fluids (mineral oil, solubles, synthetic, and semi- synthetics) and of quartz and cristobalite polymorphs of crystalline silica.

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

- **Project Title: EFFECT OF IL-1 AND TNF ON ELASTIN PRODUCTION IN COPD**

  Principal Investigator & Institution: Goldstein, Ronald H.; Professor; Medicine; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 02118

  Timing: Fiscal Year 2001; Project Start 29-SEP-2000; Project End 31-AUG-2004

  Summary: (adapted from the applicants' abstract) **Emphysema** is defined as an abnormal enlargement of the respiratory spaces with destruction of the alveolar wall. Loss of elastic recoil of the lung and loss of alveolar attachments to small airways cause irreversible airway obstruction. Epidemiological evident suggest that the disease develops because of complex interactions between inflammatory events, alveolar structures and repair processes. Accumulating evidence suggest that repair processes involving elastin resynthesis by myofibroblasts limit alveolar damage and perhaps restore alveolar units. This proposal will focus on the inflammatory processes that hinder the repair of the alveolar matrix following injury. The investigators' preliminary data reveal that interleukin1 (IL-1) and tumor necrosis factor-(TNF-) down-regulate elastin mRNA and subsequently reduce the accumulation of elastin in the extracellular matrix by lung fibroblasts in culture. These mediators are present in the alveolar space following lung injury and thus may impair elastin production in the alveolar wall. IL-1 decreases the rate of transcription of the elastin gene by more than 80 percent as determined by nuclear run-on assays. Transient transfection experiments indicate that IL-1 and TNF- function through cis- acting elements in the proximal elastin promoter. Electrophoretic gel shift assays utilizing nuclear proteins isolated implicate C/EBP-proteins and an unidentified zinc finger type protein in mediating this down-regulation.

Mice deficient in TNF- receptors (double receptor knockout) sustained less injury following intratracheal elastase administration as assessed by measurements of tissue density. The investigators will determine the molecular mechanisms whereby these effector substances regulate elastin transcription. The investigators will investigate the signaling pathway utilized by IL-1 and TNF- to decrease elastin transcription. The investigators postulate that this down-regulation of elastin production limits lung repair in vivo. The investigators will test their hypothesis using wild-type and IL-1 and TNF-receptor knockout mice treated with intratracheal pancreatic elastase administration or exposure to cigarette smoke. These studies will provide new insights into the pathogenesis of **emphysema** and suggest new treatment options.

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

- **Project Title: EFFECTS OF KLOTHO PROTEIN ON AGING AND METABOLISM**

  Principal Investigator & Institution: Kuro-O, Makoto; Pathology; University of Texas Sw Med Ctr/Dallas Dallas, Tx 753909105

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

  Summary: (Provided by applicant): With a significant increase in the average life span during last century, more and more people are facing old age and diseases associated with aging. By elucidating the mechanisms of aging, it may eventually become possible to delay the deleterious effects from old age through rational drug intervention. Because the phenotype of mice deficient in Klotho protein suggests that Klotho suppresses aging, identification of the Klotho protein function may provide new insights into the mechanisms behind aging required to achieve this long-term goal. Klotho-deficient mice exhibit a syndrome resembling human aging such as a shortened life span, arteriosclerosis, osteoporosis, skin atrophy, ectopic calcification, lipodystrophy, and pulmonary **emphysema.** Consequently, the klotho mouse becomes the first laboratory animal model of human aging caused by a single gene mutation. Recent evidence suggests that Klotho protein functions as a humoral factor that inhibits insulin signaling and reduces oxidative stress. Interestingly, these two effects of Klotho are identical with the two evolutionally conserved mechanisms that can suppress aging in lower animals. The proposed mechanism of Klotho action is that Klotho binds to its putative cell-surface receptor and sends a signal into the cell to inhibit insulin signaling and suppress oxidative stress, which eventually suppresses aging in mammals. The objective of this proposal is to test this hypothesis. Specific aims are to: (1) Determine the mechanism by which Klotho inhibits insulin action. Phenotypic consequence of Klotho-deficient mice whose insulin-signaling pathway is chronically inhibited is also determined. If inhibition of insulin signaling is essential to the anti-aging effect of Klotho, the aging phenotypes would be improved in these mice. (2) Determine the mechanism by which Klotho reduces oxidative stress. Phenotypic consequence of Klotho-deficient mice overexpressing an enzyme that detoxifies reactive oxygen species is also determined. If reduction in oxidative stress is essential to the anti-aging effect of Klotho, the aging phenotypes would be improved in these mice. These studies would provide the first genetic evidence for the involvement of insulin signaling and oxidative stress in mammalian aging. (3) Identify Klotho receptor. Identification of Klotho receptor is indispensable to elucidating intracellular Klotho-signaling pathway. In addition, it promises to promote better understanding of the Klotho protein function and verify its role as an anti-aging hormone, which would have a significant impact on basic research and medical practice of aging.

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

- **Project Title: EFFECTS OF TOBACCO SMOKE ON AIRWAY BACTERICIDAL ACTIVITY**

  Principal Investigator & Institution: Di, Yuan-Pu P.; Environ & Occupational Health; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 18-SEP-2002; Project End 31-JUL-2005

  Summary: (Taken from the Investigator's Abstract) Environmental stresses such as microorganisms and toxic chemicals have profound effects on lung injury and pulmonary disease. Airway bacterial infection has been associated with various lung diseases such as pneumonia, cystic fibrosis, and tuberculosis. Tobacco smoke (TS) is known to induce pulmonary diseases such as **emphysema** and lung cancer and has effects on the host defense mechanism against pathogens, but the molecular mechanisms by which this occurs is not completely understood. The long-term goal of this proposal is to investigate the functional characteristics of a novel airway specific gene, DD4, its regulation and its potential role in health and human lung diseases that relate to tobacco smoke. The human DD4 gene is specifically expressed in serous cells of submucosal glands where bactericidal proteins such as lysozyme and lactoferrin are secreted. This novel gene has exhibited significant response to promoting agents of mucous cell differentiation such as UTP and retinoids, as well as to several mediators of inflammation and proliferation such as tumor necrosis factor-alpha (TNF-alpha) and epidermal growth factor (EGF). Of potential significance, the candidate?s preliminary studies revealed that DD4 has antibacterial properties and that its secretion varied dramatically between different lung diseases. In addition, the candidate?s laboratory also observed that human DD4 MRNA expression is elevated upon TS stimulations in both time and dose dependent manner. The objective of this application is to elucidate effects of TS on the regulatory mechanism of DD4?s gene expression and to examine DD4?s function after TS exposure both in vitro and in vivo. The central hypothesis to be tested is that DD4 is a secreted bactericidal protein that plays a role in airway defense mechanisms against pathogens. The rationale behind this research is that modulation (such as TS exposure) of the secretary DD4 protein is one means of directly affecting host defense response against human airway infection. Therefore, regulation of DD4 gene expression and protein secretion in response to pathological stimuli must be understood before the mobilization of host defenses and the pathogenesis of airway diseases that are related to DD4 can be fully appreciated. To accomplish the objectives of this application, they will pursue three specific aims: (1) to characterize the bactericidal activity of DD4; (2) to elucidate the regulatory mechanism of TS exposure on DD4?s bactericidal function; (3) to evaluate DD4?s antibacterial effect in vivo. At the completion of this research, the candidate expects to have determined the bactericidal potency of DD4 and the regulation by TS of the antibacterial defense mechanism of DD4. The candidate expects that regulation of DD4 will prove to be related, at least in part, to the inflammatory response and tobacco smoke exposure. Finally, the candidate may obtain a better understanding of the pathogenesis of bacterial infections in certain lung diseases under effects of tobacco smoke, and the development of new therapeutic strategies.

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

- **Project Title: EGF RECEPTOR SIGNALLING IN ELASTASE INITIATED LUNG INJURY**

  Principal Investigator & Institution: Panchenko, Mikhail P.; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 02118

  Timing: Fiscal Year 2002; Project Start 20-DEC-2001; Project End 30-NOV-2006

Summary: Pulmonary **emphysema** is a progressive disabling disorder in humans characterized by destruction of the alveolar walls in enlargement of the peripheral airspaces in the lung. Protease/anti-protease imbalance significantly contributes to the pathogenesis of pulmonary **emphysema.** Proteolytic processing of extracellular matrix (ECM) and cell surface molecules by serine proteases and metalloproteinases (primarily of neutrophil and macrophage origin_ involves a variety of receptor- mediated intracellular significant events which regulate gene expression and affect proliferation, migration, differentiation, as well as viability of the injured cells. After injury inadequate repair of damaged lung tissue results in remodeling of airways and organ dysfunction. In preliminary studies we found that neutrophil elastase (NE) induces the down-regulation of EGF receptor (EGFR) and activation of extracellular signal regulated kinases 1 and 2 (ERK) in vitro in cultured pulmonary fibroblasts and in vivo of the injured lung. We also found that NE- initiated signaling leads to the decrease of elastin mRNA in cultured cells. We hypothesize that the NE-initiated EGFR-mediated ERK pathway can suppress elastin re-synthesis in NE-injured lung, and thus contribute to the progression of pulmonary **emphysema,** Our current working model predicts that NE by degrading specific ECM components releases the cell surface anchored EGFR to initiate its endocytosis and signaling towards ERK. The focus of Project 3 will be to determine the mechanism of NE-initiated EGFR-mediated ERK activation in cultured lung fibroblasts and to examine the impact of this signaling pathway on the progression of NE-induced **emphysema** in mice. Three specific aims are proposed. 1. Determine the mechanism of NE-initiated EGFR down- regulation and signaling in pulmonary fibroblasts. 2. Investigate the role of EGFR signaling pathway in elastogenic, proliferative, and apoptotic responses of NE-injured pulmonary fibroblasts; 3. Examine the role of EGFR signaling in an animal model of NE-induced pulmonary **emphysema.**

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

- **Project Title: ELASTIN GENE MUTATIONS: MECHANISMS CAUSING SVAS AND ADCL**

  Principal Investigator & Institution: Urban, Zsolt; None; University of Hawaii at Manoa 2500 Campus Rd Honolulu, Hi 96822

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

  Summary: (provided by applicant): The overall goal of this proposal is to explore the functionally distinct pathomechanisms by which mutations in the elastin gene (ELN) result in the two phenotypically different heritable human disorders, supravalvular aortic stenosis (SVAS) and autosomal dominant cutis laxa (ADCL). In our preliminary data we provide evidence indicating that obstructive vascular disease in SVAS is caused null mutations in the elastin gene and that the resulting reduction of elastin deposition is associated with a hyperproliferative cellular phenotype. In ADCL patients, in contrast, we have identified mutations that result in the expression of mutant tropoelastin. Based on these results, we hypotesize that different classes of elastin gene mutations result in SVAS and ADCL by disrupting either the growth regulatory or the mechanical function of elastin through distinct pathomech an isms. To test this hypothesis, we propose (1) a mutational analysis of the elastin gene (ELN) and genotype-phenotype association studies in a cohort of SVAS and ADCL patients, (2) functional analysis of the mutations in cultured cells form SVAS and ADCL mutations, (3) further functional studies by expressing wild type and mutant elastin minigenes in immortalized pigment epithelium and skin fibroblast cells and (4) generation of a transgenic model of ADCL by introducing selected mutant elastin minigenes into mice. The studies proposed here take advantage of the unique existence of two genetic disorders in which alternative

functions of elastin are disrupted by different types of mutations within ELN. These experiments therefore will allow for the genetic dissection of the different roles elastin plays in elastic tissue. Our studies will lead to the elucidation of the pathomechanism of SVAS and ADCL which may be used for better diagnosis and treatment of these diseases. Finally, we expect to gain a better understanding of the pathomechanisms of common diseases that are found in association with ADCL such as hernias, **emphysema** and arterial aneurysms.

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

- **Project Title: EMPHYSEMA: OUTCOMES AND TECHNOLOGY ASSESSMENT**

  Principal Investigator & Institution: Yusen, Roger D.; Medicine; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2001; Project Start 10-JAN-2000; Project End 30-NOV-2004

  Summary: This project seeks to improve outcomes in patients with **emphysema.** Therapies such as lung volume reduction surgery (LVRS) and lung transplantation (LTx) offer potential improvements in quality of life, but they impose substantial risks. Thus, decision making about the use of LVRS and LTx requires trade-offs. Rational analyses of these trade-offs require valid measurements of the benefits and harms to the patients in all relevant domains that effect duration and quality of life, including morbidity, functional status, symptoms, and satisfaction. We do not have an agreed upon standard of successful therapy, specifically in situations where duration of survival is not the only issue. The instruments we use to assess procedures may not fully capture the aspects of health and quality of life that are most important. New instruments and models for assessing outcomes are necessary to complement those that exist. The specific aims of this project are 1) to further develop methods to assess outcomes of patients with **emphysema,** and 2) to assess the effects of lung volume reduction surgery and lung transplant on outcomes of patients with **emphysema.** The effects of therapies on mortality and quality of life, measured as utilities, will be assessed. Patient demographics, co-morbidity, functional status, symptoms, and satisfaction, as well as intermediate physiologic outcomes, and utilization of resources will be measured. To achieve the specific aims, primary data collection will be performed in three ways: instrument validation, cross-sectional and (pre and post-operative) longitudinal studies. Models of the relationships among functional status, satisfaction, physiology, and quality of life in patients with **emphysema** will be developed and used to explain the relationships among the various outcomes. We will also develop operational definitions of successful and unsuccessful treatments among patients with **emphysema** undergoing LVRS or LTx that account for functional status, satisfaction, physiology, and quality of life, as well as mortality. Prediction rules for outcomes among patients with **emphysema** undergoing LVRS or LTx will be developed. This research plan promotes the development of methods for assessing and understanding the role of new technologies and therapeutic interventions in patients with **emphysema.**

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

- **Project Title: ENDOTHELIAL CELL DEATH AND INFLAMMATION IN EMPHYSEMA**

  Principal Investigator & Institution: Tuder, Rubin M.; Associate Professor; Pathology; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2001; Project Start 29-SEP-2000; Project End 31-AUG-2004

Summary: (adapted from the applicants' abstract) **Emphysema** is caused by a loss of alveolar lung structures. For the purpose of this application, the investigators focus on one important aspect of inflammation: oxidant stress. The investigators believe that the oxidant stress, such as induced by inflammation in chronic obstructive pulmonary diseases, compromises the endothelial and epithelial molecular programs that ultimately maintain the structural and cellular integrity of the adult human lung. The investigators hypothesize that the disappearance of lung alveoli in centrilobular **emphysema** occurs by apoptosis of capillary endothelial cells due to decreased expression of lung Vascular Endothelial Growth Factor (VEGF) and its receptor KDR. The investigators also propose that oxidant stress (oxidants, reactive oxygen or nitrogen species), that may be induced by lung inflammation, or in lung resident cells, causes lung endothelial cell death after interruption of VEGF/KDR survival signaling. The investigators' experimental approach relies on inhibition of KDR by the specific inhibitor SU5416 (from SUGEN Corp.). The specific aims of this proposal are: 1) to determine whether chronic blockade of the VEGF-receptor KDR with SU5416 causes **emphysema** in rats. The investigators will also investigate whether SU5416- induced **emphysema** involves endothelial cell death, lung inflammation, and oxidant stress. The investigators will also address whether caspase inhibition prevents **emphysema** induced by SU5416; 2) to determine whether oxidant stress causes endothelial cell death and **emphysema.** The investigators will also determine whether oxidant stress decreases VEGF gene expression or modified KDR posttranslationally and whether it enhances the effect of SU5416 in rat lung; and 3) to determine whether scavenging lung oxidants with a SOD mimetic prevents the development of **emphysema** caused by KDR blockade or lung oxidant stress. The investigators' approach is to investigate rat models of **emphysema** caused by KDR receptor blockade or oxidant stress, to quantify the extent of **emphysema** using the mean linear intercept and functionally characterize the lung using pressure/volume curves, to assess lung alveolar septal endothelial cell death and lung caspase activity, to assay the lung tissue for several markers of oxidant stress (nitrotyrosine, products of lipid peroxidation, isoprostanes, carbonyl proteins). In cultured endothelial cells, the investigators will investigate in depth whether oxidant stress causes nitrosylation of the KDR receptor and thus alters KDR signaling. The investigators believe that the in depth exploration of these models will render results that are highly relevant to the human condition. The experimental results may point the way towards a new treatment/prevention strategy, i.e., inhibition of lung alveolar septal endothelial cell apoptosis and oxidant stress.

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

- **Project Title: EPIDEMIOLOGIC STUDIES OF LUNG CANCER RISKS IN NSAID USERS**

  Principal Investigator & Institution: Zheng, Wei; Professor; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

  Timing: Fiscal Year 2001; Project Start 28-JUN-2001; Project End 31-DEC-2006

  Summary: (provided by applicant): Cumulative evidence from in vitro and animal studies suggests that the enzyme cyclooxygenase-2 (COX-2) is important in the development and progression of lung cancer. Epidemiologic studies evaluating the association between the use of aspirin (an inhibitor of COX-2) and the risk of lung cancer have been conflicting, and no study has been conducted to evaluate non-aspirin non-steroidal anti-inflammatory drugs (NSAIDs). Using pre-recorded drug prescription databases of the Tennessee Medicaid program and North Jutland County of Denmark, we propose to conduct two studies in these populations to examine the effect of NSAID

use on the risk of lung cancer. The first is a retrospective cohort study of over 10,000 enrollees of the Tennessee Medicaid Program who were diagnosed with chronic obstructive pulmonary diseases (COPD) during the period of 1980 to 2002. The second is a population-based, retrospective cohort study of over 150,000 users of NSAIDs in the general population of North Jutland County during the period of 1991 to 2002. Within the Danish cohort will be a nested case-control study of 350 cases and 700 controls, in which relevant information will be obtained on over the counter (OTC) analgesic use, as well as cigarette smoking and other potential confounding factors. The two studies proposed here complement each other and provide for an international comparison of NSAIDs as possible lung cancer chemoprevention agents. Because the data on NSAID use have already been collected, the studies will be very cost-efficient. More importantly, the use of pre-recorded pharmacy records minimizes potential errors in exposure assessment and provides a major advantage over existing cohort studies in evaluating the potential chemopreventive effect of NSAIDs. Given the high incidence and mortality of lung cancer and high prevalence of NSAID use, the results from our studies may have important public health implications in lung cancer prevention, and could set the stage for future randomized trials of COX-2 inhibitors in cancer prevention.

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

- **Project Title: EPIDEMIOLOGY AND SIGNIFICANCE OF P CARINII COLONIZATION**

  Principal Investigator & Institution: Morris, Alison M.; Medicine; University of Southern California 2250 Alcazar Street, Csc-219 Los Angeles, Ca 90033

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

  Summary: (provided by applicant): The proposal will allow the candidate the opportunity to attain the following objectives: 1) To complete didactic training in clinical research, advanced statistical techniques, and epidemiology by obtaining a Masters Degree through the Clinical Research Training Program, 2) To gain laboratory experience in molecular techniques, 3) To become an independent clinical investigator focusing on the molecular epidemiology of Pneumocystis carinii and its effects on pulmonary function. The candidate will draw on the complementary expertise of 2 mentors. Joel Weissfeld, MD, MPH is an expert in epidemiology and clinical trials. Karen Norris, PhD is an expert in the molecular biology of Pneumocystis carinii. A Career Development Committee will contribute both research and career guidance. The University of Pittsburgh is a unique setting for the training of clinical researchers because of the wealth of resources available through the Pulmonary Division, the Graduate School of Public Health, the Clinical Research Training Program, and the Center for Human Genetics. The proposal will examine the molecular epidemiology of P. carinii colonization and its clinical significance. The use of the polymerase chain reaction (PCR) to detect low levels of P. carinii has improved our ability to identify colonization. We are interested in understanding the nature of P. carinii colonization and investigating its effects on pulmonary function. Preliminary data suggest that colonization may be prevalent among the HIV-infected population and in those with severe **emphysema,** but the clinical significance of such colonization is unknown. Subjects with HIV infection are at increased risk of **emphysema,** and those who have had PCP develop permanent airways obstruction. The presence of P. carinii in the lungs produces inflammatory changes similar to those seen in **emphysema.** The project will use PCR to compare rates of colonization among HIV-infected subjects, subjects undergoing lung transplantation for **emphysema** or for causes other than **emphysema,**

and normals. Clinical predictors of colonization will then be examined. Finally, degree of airways obstruction and worsening over time will be compared based on colonization status among HIV-infected subjects and smokers. This study may potentially identify a novel, treatable risk factor for susceptibility to **emphysema.** In addition, greater insight into the epidemiology of colonization may aid in understanding the transmission and prevention of P. carinii.

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

- **Project Title: FUNCTIONAL ASSESSMENT OF PULMONARY TOXICITY WITH MRM**

  Principal Investigator & Institution: Johnson, G. Allen.; Professor; Radiology; Duke University Durham, Nc 27706

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

  Summary: (Provided by Applicant): We propose continuation of studies of the environmental impact of particulate matter on lung structure and function using in vivo magnetic resonance microscopy. We will expand our previous work with hyperpolarized 3He to support localized three-dimensional structural imaging at 1 x 10-4 mm3. We will extend our physiologic support system and spiral encoding techniques to quantitative flow measurements and functional imaging at 1 x 10-2 mm3. We will study the impact of particulates in three specific models: 1) elastase-induced injury, a model of **emphysema;** 2) inflammation and remodeling in the endotoxin sensitive C3H/HeBFeJ mouse, a model of organic dust induced asthma; and 3) inflammation and remodeling in the vanadium pentoxide model of asthma, which is characterized by extensive bronchiolar fibrosis. The proposal will refine methods that will be applicable to a much wider range of basic pulmonary studies while obtaining detailed assessment of structural and functional changes in three important models of human disease. By extending the methodologies to the mouse, we will build a critical bridge between man and mouse models of pulmonary disease that will be essential to understanding the pathophysiology of pulmonary disease and the validation of new therapies.

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

- **Project Title: FUNCTIONAL GENOMIC BIOMARKERS IN COPD**

  Principal Investigator & Institution: Reilly, John J.; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 23-SEP-2002; Project End 31-JUL-2006

  Summary: (provided by applicant): Chronic Obstructive Pulmonary Disease (COPD) affects over 18 million Americans. It is clear that the major environmental risk factor for this debilitating syndrome is cigarette smoking. It is not clear, however, what factors are responsible for the fact that some smokers develop the disease while most do not. Studies of potential therapies have been hampered by the lack of easily measurable characteristics that predict the course of the disease. Most studies have used measures of lung function as a marker of disease activity. Such studies typically require large numbers of patients and an observation period of months to years. This application proposes studies to develop alternative biomarkers associated with COPD. The research proposed will develop a set of candidate biomarkers by utilizing expression array profiling to characterize gene expression patterns in lung tissue and peripheral blood associated with the presence of COPD. These candidates will then be assessed in studies performed in populations previously characterized for COPD-related phenotypes: the Boston Early Onset COPD Study and the Normative Aging Study. The initial studies

will involve expressionprofiling in both lung tissue and peripheral blood in samples obtained from patients undergoing pulmonary resections at Brigham and Women's Hospital. Samples from 20 patients with airflow obstruction on spirometry and **emphysema** demonstrated on chest CT scans will be compared to samples from 20 matched control patients. State of the art bioinformatic analytic techniques will be used to analyze these data and develop a list of candidate biomarkers based on expression differences. Polymorphisms in the candidate genes will then be studied for genetic association in two characterized populations with different disease distributions. The Boston Early Onset COPD Study consists of patients who have been diagnosed at an early age with severe COPD and their family members. In contrast, the Normative Aging Study includes participants with a broad spectrum of COPD. Studies in these populations will be directed at establishing whether differences in gene expression or gene polymorphisms are associated with COPD. It is hoped that these markers will provide insight into disease pathogenesis and serve as outcome assessment parameters.

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

- **Project Title: GAS EXCHA03NGE IMAGING IN THE LUNG USING MRI**

  Principal Investigator & Institution: Patz, Samuel; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

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

  Summary: (Adapted from the applicant's abstract): The broad objective proposed here is to develop and test a magnetic resonance (MR) method that allows functional evaluation of the lung acinar structures by measuring gas exchange. To enhance the signal, the technique uses laser-polarized (129)Xe. Laser polarization increases the signal over thermal (129)Xe by a factor of 10(4)- 10(5). (129)Xe is chosen because it is more than ten times more soluble in tissue than the remaining choice, (3)He, and because the spectral peaks from the gas and dissolved in tissue phases are separated by -200/ppm. This makes the observation of both phases easily observable. The investigators propose to measure the gas exchange rate in acinar structures by observing the relaxation recovery rate of the spectral peaks. The investigators propose to saturate the signal in the tissue (dissolved) phase and observe the signal in this phase due to exchange from the gas spaces. During the 1st year, MR methods will be optimized in phantoms and then rats, where a ventilator will be used to control the lung volume to determine if the exchange is proportional to the lung surface area, which is related to lung volume. Trial experiments on humans will be performed in the 2nd year. The surface of the alveolar septa is the site of gas exchange; its quantification in terms of the local surface to volume ratio is an important determinant of the efficiency of the lung. Derangements at this level include loss of area in destructive diseases such as **emphysema,** as well as thickening of the blood/gas barrier in interstitial diseases such as pulmonary fibrosis and edema. A major gap in clinical medicine is the failure of all current techniques to evaluate this important parameter noninvasively, or even in vivo. Gas exchange imaging represents a radically new potential for noninvasive evaluation of regional differences in pulmonary function. Early detection of the loss of alveolar surface area is a serious public health imperative, since chronic obstructive pulmonary disease is now the Th leading cause of death in the US.

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

- **Project Title: GENETIC ANALYSIS OF NICOTINE ADAPTATION IN C ELEGANS**

  Principal Investigator & Institution: Schafer, William R.; Associate Professor; Biology; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, Ca 92093

Timing: Fiscal Year 2001; Project Start 01-FEB-2000; Project End 31-DEC-2004

Summary: Tobacco use has been implicated in a wide range of human diseases, including heart disease, **emphysema,** and cancer, which together result in millions of premature deaths each year. The addictive properties of nicotine are a major cause of persistent and compulsive tobacco use. Nicotine addiction is thought to result from long-term adaptive changes in the activity and expression of nicotinic acetylcholine receptors in the brain. However, the molecular and neuronal mechanisms that underlie these adaptive processes remain poorly understood. The goal of this research is to use genetic analysis in a simple animal model, the nematode Caenorhabditis elegans, to investigate the molecular basis of nicotine adaptation. C. elegans is highly amenable to molecular analysis of nervous system function: it has a simple and well characterized nervous system, and its short generation time, small and largely sequenced genome, and accessibility to germline transformation make it ideal for classical and molecular genetic studies. C. elegans exhibits a striking and easily measurable response to nicotine, and long- term nicotine exposure leads to nicotine tolerance and dependence with respect to behaviors controlled by both neuromuscular and neuronal nicotinic receptors. In this project, genes required for nicotine adaptation in nematodes will be identified by screening for adaptation-defective mutants. Two nicotine adaptation genes identified in earlier screens will be cloned to determine their molecular functions, and to characterize the cellular pathways in which they function. The possibility, suggested by studies of protein kinase C-defective mutants, that PKC phosphorylation of nicotinic receptor subunits is a mechanism for nicotine adaptation will be tested through the analysis of transgenic worms expressing mutant receptors. The ultimate goal of this work is to provide a model for the general molecular mechanisms underlying nicotine adaptation in neurons, and to identify new proteins that participate in nicotine addiction in other animals, including vertebrates.

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

- **Project Title: GENETIC CONTROL OF SP-B GENE EXPRESSION IN THE LUNG**

  Principal Investigator & Institution: Yan, Cong; Assistant Professor; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

  Timing: Fiscal Year 2003; Project Start 20-AUG-1999; Project End 30-JUN-2007

  Summary: (provided by applicant): Surfactant protein B (SP-B) is a 79-amino acid peptide produced in pulmonary non-ciliated bronchiolar epithelial cells (Clara cells) and alveolar type II epithelial cells. The SP-B peptide is stored in lamellar bodies and secreted with phospholipids into the airway lumen to facilitate the stability and rapid spreading of surfactant phospholipids during respiratory cycles. Null mutations in the SP-B gene cause lethal respiratory distress in newborn infants and in SP-B deficient mice produced by gene targeting. SP-B is essential for postnatal alveolar maturation and respiratory adaptation in newborns. The long-term goals of this work are to identify cis-acting DNA elements and trans-acting protein factors that control SP-B gene temporal/spatial expression in developing and mature lungs. During the last several years of study, it has been identified that retinoic acid receptor heterodimer (RAR/RXR), thyroid transcription factor 1 (TTF-1), nuclear receptor co-activators (CBP/p300 and p160 co-activators, including SRC-1, TIF2 and ACTR) and signal transducers and activators of transcription 3 (STAT3) cooperatively stimulate hSP-B transcription through an enhancer region (-500 to -331 bp). To extend the study, we will 1): characterize functional domains and amino acid residues that are involved in the interaction between RARalpha and STAT3; 2) characterize RARE and TTF-1 cis-acting sites in the hSP-B enhancer region (-500 to -331 bp) that determine hSP-B gene

temporal/spatial expression in bronchiolar epithelial cells using LacZ transgenic mice; 3) characterize cis-acting elements that determine hSP-B gene temporal/spatial expression in alveolar type II epithelial cells using LacZ transgenic mice. These studies along with previous findings will lead to a better understanding of molecular basis for SP-B homeostasis in lung biology. Knowing this will help to design strategies to combat congenital and acquired respiratory diseases such as **emphysema,** respiratory distress syndrome (RDS) and bronchopulmonary dysplasia (BPD), the leading causes of mortality and morbidity in preterm infants.

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

- **Project Title: GENETICS OF COPD IN NETT**

  Principal Investigator & Institution: Silverman, Edwin K.; Assistant Professor; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

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

  Summary: (provided by applicant): Cigarette smoking is the major known risk factor for the development of chronic obstructive pulmonary disease (COPD); however, the development of airflow obstruction is widely variable among smokers. Severe alpha I-antitrypsin (AAT) deficiency is a proven genetic risk factor for COPD. In subjects without AAT deficiency, familial aggregation for COPD-related phenotypes has been demonstrated, and preliminary evidence for linkage of COPD-related phenotypes to several genomic regions has been obtained by our research group. Participants in the National **Emphysema** Treatment Trial (NETT) provide an extremely valuable resource to identify novel COPD susceptibility genes. NETT participants provide a group of relatively homogeneous COPD patients, because all subjects have severe **emphysema.** However, within the NETT population, there are significant differences in the distribution of **emphysema** and the response to Lung Volume Reduction Surgery (LVRS). We propose to obtain blood samples for DNA extraction from NETT patients; we will use these DNA samples along with the extensive phenotypic assessment of NETT patients to test candidate genes as contributors to COPD susceptibility. Candidate gene polymorphisms, selected from regions of COPD linkage, animal models of COPD, and prior case-control association studies, will be tested between subgroups of NETT patients to determine if these genes contribute to differences in **emphysema** distribution and clinical response to LVRS. These polymorphisms will also be compared in NETT patients and a population-based control sample to test candidate genes for association with COPD susceptibility. Although previous case-control genetic association studies in COPD have provided inconsistent results, the application of new approaches to test for population stratification, the use of adequate sample sizes, and correction for multiple comparisons will provide a robust study design.

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

- **Project Title: HE3 MR DIFFUSION & LOW DOSE CT QUANTITATION OF EMPHYSEMA**

  Principal Investigator & Institution: Gierada, David S.; Radiology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2002; Project Start 23-SEP-2002; Project End 31-JUL-2006

  Summary: (provided by applicant): The goal of this proposal is to develop and evaluate hyperpolarized helium-3 diffusion magnetic resonance imaging (He-3 dMRI) and low dose quantitative computed tomography (LD-QCT) indexes of **emphysema** as noninvasive biomarkers for the presence, severity, and progression of **emphysema.**

Emphysema is a pathologic abnormality of the lungs defined by enlargement of terminal airspaces and destruction of airspace walls, and is commonly present in the millions of patients with chronic obstructive pulmonary disease. Increased knowledge regarding the role of inflammatory mechanisms and proteinases in the pathogenesis of COPD is leading to searches for newer anti-inflammatory strategies and enzyme inhibitors. Though in the early stages of development, some of these new approaches may eventually provide therapy that alters the course of the disease. Accurate biomarkers of **emphysema** would allow for early diagnosis, intervention, and evaluation of new therapies. Though spirometry is used to diagnose COPD, it is a relatively inaccurate means of assessing for **emphysema.** Conventional CT is a highly accurate way to assess the severity of **emphysema,** which can be quantified by the decrease in x-ray attenuation of the lungs that results from airspace enlargement and alveolar destruction. However, CT is performed using relatively high doses of ionizing radiation, which limits its acceptability as a screening and follow-up test, particularly in early or mild disease. In recent years, other noninvasive imaging tests for **emphysema** have been designed that require no or greatly reduced ionizing radiation. One new test, He-3 dMRI, uses a specially constructed MRI pulse sequence to measure the degree to which diffusivity of inhaled hyperpolarized He-3 gas is restricted by alveolar walls. This measurement, the apparent diffusion coefficient (ADC), is increased (gas diffusion is less restricted) when alveolar spaces are enlarged in **emphysema.** Another test, low dose CT scanning, allows depiction of substantial lung detail at less than 20 percent of the radiation dose of conventional CT, but has not been developed for quantitation of **emphysema.** Though promising, the optimal technique and validity of both He-3 dMRI and LD-QCT have yet to be established. We hypothesize that 1) Optimizing He-3 dMRI and LD-QCT techniques will allow sensitive and accurate assessment of **emphysema,** compared to lung morphometry, 2) The optimized He-3 dMRI and LD-QCT techniques will provide valid biomarkers of **emphysema** that can be applied to other populations, and 3) He-3 dMRI and LD-QCT will allow identification of **emphysema** progression over time. We will study three separate groups of subjects. In the first group, we will determine which scanning and analysis parameters provide ADC and LD-QCT biomarkers that most accurately quantify the amount of **emphysema** present pathologically in lobectomy specimens (Aim I). We will then use the optimized scanning and analysis techniques to validate these measurements in a different group, compared to the amount of **emphysema** present in lobectomy specimens (Aim II). In a third group of subjects, we will determine ADC and LD-QCT lung attenuation measurements at serial time points to assess for **emphysema** progression (Aim III).

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

- **Project Title: IL-13, MYOFIBROBLASTS & ELASTIC RECOIL IN SEVERE ASTHMA**

  Principal Investigator & Institution: Wenzel-Morganroth, Sally E.; Professor; National Jewish Medical & Res Ctr and Research Center Denver, Co 80206

  Timing: Fiscal Year 2001; Project Start 20-SEP-2001; Project End 30-JUN-2006

  Summary: (provided by applicant): The pathophysiology of severe asthma is poorly understood. A subset of patients with severe asthma, who are predisposed to near fatal events appears to have increases in airway collapsibility and loss of elastic recoil contributing to their severity. We hypothesize that these changes are driven by inflammatory and structural changes in the distal lung which involve the transformation of fibroblasts to myofibroblasts. The associated injury and repair process, involving mast cell proteases and metalloproteinases (MMP), alone or in combination, cleaves elastin and other extracellular matrix (ECM) components. The breakdown

products of ECM, in turn, feed back on the myofibroblasts continuing the cycle of elastin production, MMP release/activation and elastin breakdown. These changes alter the alveolar-parenchymal attachments, decreasing elastic recoil and markedly worsening the clinical severity of the asthma. In Specific Aim 1 we will characterize physiologic parameters felt to be important in asthma: airflow limitation, bronchial hyperreactivity, and, in addition, elastic recoil (measured by pressure-volume curves). The asthmatic subjects will undergo endobronchial and transbronchial biopsy to evaluate the cellular and immune inflammatory process in both lung compartments. Resected lung from **emphysema** patients will be used for comparison. High resolution CT scans will evaluate parenchymal differences among the groups. Specific Aim 2 will measure elastin in the distal lung of the subject groups and the relationship to myofibroblast phenotypic changes. These changes will be compared to MMP and mast cell protease amounts and activity, as well as ECM degradation products in the distal lung. In Specific Aim 3, we will develop an in vitro model of the observed in vivo processes by culturing fibroblasts from proximal and distal lung. Cellular interactions between growth factors, proteases and extracellular matrix will be specifically evaluated. Completing these studies in both asthma and **emphysema** should offer new targets for the treatment and prevention of severe obstructive lung diseases.

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

- **Project Title: IMMUNE MODULATORS OF INFLAMMATION IN SEVERE COPD**

  Principal Investigator & Institution: Kheradmand, Farrah; Assistant Professor; Medicine; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

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

  Summary: Repeated injury to airways from exposure to irritants (e.g., cigarette smoke) initiates the process of airway remodeling which in some patients, can result in permanent abnormalities in lung function. Chronic airway inflammation and regulation of genes that act down stream of inflammatory mediators play a major role in the pathogenesis of airway remodeling in smokers with chronic obstructive pulmonary disease (COPD). By far the most important risk factor for development of COPD is smoking but a subset of heavy smokers will have a greater decline in lung function than expected and develop severe or end- stage COPD. While inflammatory cells have been found in the lung of smokers with COPD, the nature of "the inflammatory process" that may be key to understanding the pathogenesis of this disease remains obscure. We have found that activated T lymphocytes persist in the lungs of ex-smokers with end-stage COPD despite years of smoking cessation. Based on the literature and our own data we propose to test the hypothesis that loss of lung function in ex-smokers with end-stage COPD, is mediated through cognate immune mechanisms driven by the T helper 1 (Th1) subset of T lymphocytes. Specifically, a subset of smokers develops an aberrant lung Th1 immune response that orchestrates progressive lung destruction. Furthermore we hypothesize that ex-smokers who develop end-stage COPD can be distinguished from smokers with no or mild COPD by different patters of lung gene activation. To explore these hypotheses, in collaboration with the Houston Veterans Affairs Medical Center (VAMC) lung volume reduction surgery (LVRS) clinical trial, we plan to characterize immunological and genetic phenotypes of 12 non-atopic end-stage COPD, 24 mild COPD with **emphysema,** and 24 mild or no COPD human ex-smokers. We will determine the immune characteristics of patients with end-stage COPD by addressing the following specific aims: Aim 1) To determine the dominant immune phenotype of ex- smokers with end-stage COPD. Aim 2) To determine the mechanism of T cell activation in ex-smokers with end-stage COPD.

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

- **Project Title: INHALED PARTICLE CHARACTERISTICS AND EARLY LUNG EFFECTS**

  Principal Investigator & Institution: Beckett, William S.; Professor; Environmental Medicine; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

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

  Summary: (Adapted from the Investigator's Abstract) Chronic obstructive pulmonary disease (COPD) is a disabling condition produced by chronic bronchitis (airway inflammation and mucus hypersecretion) and **emphysema** (loss of alveolar surface area). Epidemiologic studies of the workplace have consistently shown an excess of COPD associated with dusty work environments, yet only a few substances (coal, silica, cadmium) causing COPD in the workplace have been characterized based on chemical composition and respirable particle size. These findings suggest that the much broader range of workplace dusts may in certain conditions contribute to COPD based on characteristics other than chemical composition alone. Pulmonary inflammation plays a role in early events leading to COPD. Particles less than 10 micron aerodynamic diameter are considered to be able to penetrate the upper airways and reach the respiratory tract, and are thus designated as being in the respirable range. Ambient fine particles (<2.5um) consist of two fractions: ultrafines (0.01 to 0.1 um) and accumulation mode particles (0.1 to 1.0 um). Recent studies of ambient particulates indicate that ultrafine particles may be more harmful than other fine particles on an equal mass exposure basis. In animal models, ultrafine particles have a higher alveolar deposition fraction, translocate more easily from the airways to the interstitium, induce greater activation of macrophages and cytokine release, and cause greater impairment of macrophage clearance function.One reason for the greater toxicity of equal masses of these smaller particles is their much greater surface area. We hypothesize that the size of inhaled fine particles, in addition to their chemical and other physical characteristics, plays a critical role in determining occupational health effects. To test this we will study early lung and systemic inflammatory responses as well as cardiac effects in adults after carefully controlled inhalation exposure to ultrafine and accumulation mode zinc oxide, a particle we have previously characterized for the dose-response relationship of its short term pulmonary and systemic inflammatory effects. Studies will be conducted in the Environmental Exposure Facility of the Adult General Clinical Research Center. We will compare ultrafine to larger, accumulation mode particles (on an equal mass exposure basis) in their ability to produce symptoms, fever, markers of airway inflammation, antioxidants, systemic acute phase proteins, and alterations in the blood clotting cascade, cytokine release, heart rate, rhythm, and repolarization. We anticipate that the results will help to determine whether there are differential effects for equal mass exposures to fine particles of different size fractions in the pathogenesis of COPD

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

- **Project Title: INTEGRATION BY AIRWAY PARASYMPATHIC GANGLIA NEURONS**

  Principal Investigator & Institution: Myers, Allen C.; Medicine; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2001; Project Start 01-APR-1992; Project End 31-MAY-2005

  Summary: In the airway, the autonomic nervous system controls smooth muscle tone, secretion by glands, and blood flow. Although there is abundant physiological and

pharmacological evidence indicating that dysfunction of this autonomic control of the airways contributes to the causes and symptoms of pulmonary diseases such as bronchial asthma, chronic obstructive pulmonary disease and **emphysema,** little is actually known about the regulation of these nerves. Our long term goal is to provide knowledge of how autonomic tone is regulated in the airway, especially that provided by the parasympathetic nervous system. Control of smooth muscle in the trachea and bronchi is predominantly by nerve fibers that emanate from neuronal cell bodies in parasympathetic ganglia, small clusters of cell bodies located near the airway wall. The parasympathetic tone of the airway smooth muscle is thought to be under the control of the central nervous system where signals are transmitted rhythmically during respiration to the parasympathetic neurons in the airway wall. This signal activates airway parasympathetic ganglia neurons by release of a neurotransmitter which mediates cholinergic synaptic transmission in the ganglia. Separate, but potentially important, forms of neural regulation of parasympathetic neurons in the airways are by the so-called local peripheral reflex pathway and the intraganglionic pathways. In the peripherals reflex pathway, a sensory nerve is activated by changes in the airway and communicates directly with the parasympathetic neuron in the nearby ganglia by releasing neuropeptides from branches of the sensory axon, evoking non-cholinergic synaptic transmission. In other words, this is an sensory- parasympathetic reflex, independent of the central nervous system. A peripheral reflex would thus allow local increases in parasympathetic tone in an airway segment, independent of changes in another segment. In the intraganglionic pathway, postganglionic axons leaving a bronchial ganglion serve to innervate, and modulate the function of neighboring ganglia within the airway tree. This proposal describes experiments that will address our central hypothesis, namely that the parasympathetic nerve activity in the airways is shaped by the integration of three separate inputs: 1.) input from the central nervous system {classical cholinergic nicotinic input), 2.) input from the peripheral reflex sensory fibers, and 3.) input from surrounding postganglionic parasympathetic ganglia. We feel that an understanding of the mechanism of this integration is a prerequisite to obtaining knowledge on the mechanisms by which airway neurophysiology is regulated in health and disregulated in disease.

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

- **Project Title: LIVING RELATED PULMONARY LOBAR TRANSPLANTATION**

  Principal Investigator & Institution: Kron, Irving L.; Professor; Surgery; University of Virginia Charlottesville Box 400195 Charlottesville, Va 22904

  Timing: Fiscal Year 2001; Project Start 01-JAN-1993; Project End 31-MAR-2002

  Summary: (Adapted from the applicant's abstract) Clinical lung transplantation has developed over the past several years into a viable therapeutic option for many types of end-stage lung disease. Most patients benefiting from this therapy are adults with various types of end-stage **emphysema,** primary pulmonary hypertension, restrictive lung disease such as pulmonary fibrosis, and cystic fibrosis. Relatively few children are in need of lung transplantation, and because of a lack of donor organs, fewer still actually undergo this life-saving surgery. In 1995, nearly one-third of children on the lung transplant waiting list died while waiting a suitable organ. The investigators and others have already reported on the experimental and clinical application of "reduced size" lung transplantation in which part of a more mature lung is transplanted into a smaller recipient in order to identify more donor organs for the pediatric population. Previous work on this project focused on examining the long-term functional results of reduced-size transplants and whether or not they were superior to size-matched

immature whole lung transplants. In addition, the authors briefly began to identify the growth potential of reduced-size lung transplants, but only at a whole-organ level. It was found that a mature lobe transplanted into an immature recipient does have the ability to grow. The stimulus for and the cellular basis of this lung growth are unknown and are the focus of continued research. Studies will continue to be done in a porcine model of lung transplantation with which we are very familiar. New studies propose to identify factors present in the immature host environment which are responsible for lung growth and differentiation and how they may stimulate further growth of an already mature lobar transplant. Pneumocyte division and differentiation potential will also be examined. The time course and molecular modulation of normal pig lung growth and development will be studied to allow further interpretation of experimental results in the transplanted lungs. In addition, the effects of chronic rejection on growth potential of transplanted lungs will also be examined at the cellular and whole organ level. Identification of molecular modulators of normal lung development and their effects on cellular events of transplanted lungs will not only advance the field of lung transplantation, but will also form a basis for potential new treatments of other types of lung injury and provide a better understanding of lung growth following lung transplantation.

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

- **Project Title: LOCAL EXPRESSION OF ALPHA-1-ANTITRYPSIN IN EMPHYSEMA**

  Principal Investigator & Institution: Perlmutter, David H.; Professor; Pediatrics; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2001; Project Start 01-SEP-1986; Project End 31-MAY-2001

  Summary: (Adapted from Applicant's Abstract): Homozygous PIZZa1-antitrypsin (aAT) deficiency is the most common genetic cause of liver disease in children and of **emphysema** in adults. This deficiency is associated with a misfolding by functionally active aATZ molecule which is retained in the endoplasmic reticulum (ER) rather than secreted into the blood and body fluids. Lung injury is due to the decrease in a1AT molecules available in the lung to inhibit neutrophil elastases. Liver injury is due to the hepatotoxic effect of the misfolded a1AT molecule retained in the ER. The investigator has observed that a subgroup of PIZZ individuals may be more susceptible to liver injury by virtue of co-inherited variants in the quality control apparatus of the ER which is responsible for recognition and degradation of misfolded proteins. The investigator has also found that the proteasome plays a key role in the degradation of a1ATZ. More recent studies have shown that the classical autophagic response also plays a role in response to, and degradation of a1-ATZ. In addition, the investigator has evidence which suggests that exogenous chemical chaperones can at least partially reverse the folding defect of a1-ATZ and at least on of these, 4-phenylbutyric acid, is an excellent candidate for chemoprophylaxis of both liver and lung disease in a1-AT-deficiency. In addition, the investigator has also observed that several inhibitors of carbohydrate processing, castanospermine and kifunensine, also mediate increased secretion of a1ATZ. Thus, in the renewal application, the investigator proposes to focus on the effects of chemical chaperones and inhibitors of carbohydrate processing on mutant a1-AT-deficient patients. The investigator also plans to continue the studies of proteolytic mechanisms which determine the fate of a1-ATZ in the ER and of specific, presumably protective, signal transduction pathways that are activated by the retention of a1-ATZ in the ER. Lastly, the investigator proposes to determine whether there are tissue-specific differences in ER retention of a1-ATZ and the autophagic response in the lung and liver of PiZ mouse in vivo during homeostasis and inflammation.

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

- **Project Title: LUNG CONNECTIVE TISSUE-RESPONSES TO INJURY AND REPAIR**

  Principal Investigator & Institution: Foster, Judith A.; Associate Professor of Biochemistry; Biochemistry; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 02118

  Timing: Fiscal Year 2002; Project Start 03-DEC-1991; Project End 30-NOV-2006

  Summary: The central theme of this Program Project is directed toward elucidating mechanisms underlying the response of the lung to elastase injury-a situation clinically relevant to the development of COPD. Our hypotheses is that elastase-induced degradation of lung tissue results in a change in the viability of elastogenic cells and their phenotypic dependent on the proximity to and duration of elastase injury and exposure to matrix-released growth factors and secreted cytokines. Normally these processes result in localized repair of elastin without inducing a general fibrotic response. However, the loss of elastin combined with release of matrix bound growth factors and cytokines can lead to chronic release or elastase resulting in inefficient elastin repair and subsequent destruction of tissue integrity. This renewal application builds on the accomplishments of the last funding period and proposes to expand our hypotheses to gain new insights into mechanisms underlying the response of lung to elastase injury. To pursue investigation of this central theme four Projects will address the overall hypothesis from common conceptual objectives with different experimental designs. Al four projects propose an integrated approach that combines in vitro culturing of pulmonary cells to understand mechanisms and in vivo animal model to test and further understand these mechanisms. The aims and experimental design of each project are intertwined to allow maximum interchanges of expertise and technical assistance. Dr. Foster will investigate the factors responsible for transcriptional up-regulation of the elastin gene in situations related to elastase injury. Dr. Nugent will investigate the role of proteoglycans in modulating the release and receptor binding of matrix bound growth factors. Dr. Pancenko will study the role of EGF receptor signaling in elastase-induced injury. Dr. Goldstein will study the effects of the cytokines, tumor necrosis factor- and interleukin 1beta, on elastin gene transcription and cell apoptosis. The four Projects will be supported by a Core facility that will provide central administrative services, cell cultures, microscopic analyses, and the implementation analyses, and the implementation and assessment of common animal experiments. Together, over the requested five years, we hope to contribute to the understanding of the mechanisms that underlie t he pathological events leading to the clinical manifestations of **emphysema.**

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

- **Project Title: LUNG HEALTH STUDY--LONG TERM FOLLOW UP**

  Principal Investigator & Institution: Altose, Murray D.; Chief of Staff (W); Medicine; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

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

  Summary: The Lung Health Study (LHS), conducted from 1986-1994, demonstrated that a smoking intervention program in middle-aged long-term cigarette smokers can result in a highly significant beneficial effect on the rate of FEV1 decline over five years. However, FEV1 is only a surrogate marker for clinical outcomes of respiratory morbidity and mortality. The present study proposes long-term post-trial follow-up of

former LHS participants to assess the incidence of morbidity and mortality from respiratory and cardiovascular diseases and other causes, as documented by hospital, clinic, and death records. A pulmonary function test 11 to 12 years after entry into the LHS is also proposed to determine long- term effects of the LHS smoking intervention program on lung function. The main objectives of the study are as follows: 1) to determine, using an intent-to-treat analysis, whether the LHS smoking intervention significantly reduces the incidence of clinically important respiratory and cardiovascular disease over a 12- to 15-year period following study enrollment; 2) to determine whether the beneficial effect of the smoking intervention program on measures of lung function persists through 11 to 12 years of follow-up; 3) to estimate the magnitude of the effects of FEV1 and FVC on the risks of cardiovascular and respiratory morbidity and mortality, after controlling for smoking history; 4) to study the role of other factors (gender, airways reactivity, weight gain, and co- morbidities) in determining the rate of decline in pulmonary function and the risks of cardiovascular and respiratory morbidity and mortality. All ten of the original LHS clinical centers plan to participate. To minimize bias, all surviving participants of the LHS will be invited to participate, giving a potential sample size of 5600.

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

- **Project Title: LUNG HEALTH STUDY--LONG TERM FOLLOW-UP**

  Principal Investigator & Institution: Bailey, William C.; Professor and Director; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

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

  Summary: The Lung Health Study (LHS), conducted from 1986-1994, demonstrated that a smoking intervention program in middle-aged long-term cigarette smokers can result in a highly significant beneficial effect on the rate of FEV1 decline over five years. However, FEV1 is only a surrogate marker for clinical outcomes of respiratory morbidity and mortality. The present study proposes long-term post-trial follow-up of former LHS participants to assess the incidence of morbidity and mortality from respiratory and cardiovascular diseases and other causes, as documented by hospital, clinic, and death records. A lung function test 11 to 12 years after entry into the LHS is also proposed to determine long-term effects of smoking cessation on lung function. The main objectives of the study are as follows: 1) to determine, using an intent-to-treat analysis, whether the LHS smoking intervention significantly reduces the incidence of clinically important respiratory cardiovascular disease over a 12- to 15-year period following study enrollment; 2) to determine whether the beneficial effect of the smoking intervention program on measures of lung function persists through 11 to 12 years of follow-up; 3) to estimate the magnitude of the effects of FEV1 and FVC on the risks of cardiovascular and respiratory morbidity and mortality, after controlling for smoking history; 4) to study the role of other factors [gender, airways, reactivity, weight gain, and co- morbidities] in determining the rate of decline in pulmonary function and the risks of cardiovascular and respiratory morbidity and mortality. All ten of the original LHS clinical centers plan to participate. To minimize bias, all surviving participants of the LHS will be invited to participate, giving a potential sample size of 5600.

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

- **Project Title: LUNG IMAGE DATABASE**

  Principal Investigator & Institution: Meyer, Charles R.; Professor; Radiology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

Timing: Fiscal Year 2001; Project Start 17-AUG-2001; Project End 31-JUL-2006

Summary: (provided by applicant) This proposal is a response to RFA CA-01-001, Lung Image Database Resource for Imaging Research. Herein we propose to participate in formulating the multi-institutional lung imaging database acquisition and quality control specification, and begin collecting cases and populating a local database according to the specification resulting from the multi-institutional consensus guidelines. The database will be served for public sharing either through direct Internet access from our lab, or via NIH centralized resources as determined later. We believe that there are multiple reasons why we should be chosen as one of the institutions to participate in this project. 1) We have been participants, at times leaders, in the fields of image processing that this database is designed to advance. These fields include computer assisted diagnosis (CAD) of cancer from mammograms and now applied to CT scans, detection of metastatic and primary cancer changes in response to chemo and radiation therapy via registration and subtraction of interval CT exams, and the use of CT side information to reduce PET?s overall system point spread function to improve quantitative analysis of lesions smaller than 1 cm. Such prior expertise will insure that database acquisition specifications contain nearly all necessary elements required for future use. 2) The clinical collaborators on this project have already had significant experience recruiting lung patients for another lung database project, the National **Emphysema** Treatment Trials (NETT). In this project Michigan ranked second in the number of patients screened for the study, and first in the enrollment of patients that passed the screen. 3) The design of patient research database construction methodology that safely cleans patient identifiers from the data has already been completed for a pending POl application. 4) The Department of Radiology and the University Hospitals are already committed to the acquisition of new generation CT and PET scanners within the next 2 years.

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

- **Project Title: LUNG LYSYL OXIDASE REGULATION BY METAL ION HOMEOSTASIS**

  Principal Investigator & Institution: Li, Wande; Microbiology; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 02118

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

  Summary: (provided by applicant): The structural and functional integrity of the lung extracellular matrix (ECM) is largely dependent on the conversion of soluble collagen and elastin to insoluble, fibrous aggregates catalyzed by lysyl oxidase (LO), a copper [Cu(II)] dependent enzyme. This catalyst oxidizes lysine residues within these proteins to generate covalent cross-linkages stabilizing the ECM. Thus, LO plays a central role in the lung morphogenesis and tissue repair. Cadmium (Cd) is a toxic metal for humans. Inhalation and accumulation by the lung of Cd either from environmental contamination or from cigarette smoke induces perturbations of the metal ion homeostasis, which may be a key mechanism for the pathogenesis of the lung. Preliminary studies showed that development of Cd resistance (CdR) of rat lung fibroblasts (RFL6) following long-term Cd exposure was accompanied by upregulation of cellular metallothionein (MT) and glutathione (GSH), and downregulation of LO and its collagen and elastin substrates. These findings led to a hypothesis for the mechanisms of Cd injury to the lung ECM relevant to **emphysema** pathogenesis: During long term exposure to Cd, the lung fibroblasts upregulate the synthesis of MT and GSH. These intracellular thiols bind Cu ions with a higher affinity than Cd thus severely perturbing the homeostasis of Cu, limiting its availability to LO, and contributing to the

downregulation of LO at the mRNA, protein and catalytic levels as shown in preliminary studies. Downregulation of LO would in turn inhibit the crosslinking of collagen and elastin, favoring their destabilization, solubilization and eventual degradation and interfering with their repair. The resulting solubilized collagen and elastin would inhibit their own synthesis possibly by a feedback mechanism, further disturbing the balance between synthesis and degradation of these proteins and disrupting the ECM, events which are characteristic of the development of **emphysema.** The following Specific Aims are designed to test this hypothesis: 1) To assess mechanisms of Cd perturbation of Cu(ll) homeostasis in CdR-RFL6 cells; 2) To investigate mechanisms of LO downregulation at transcriptional, translational and posttranslational levels in CdR-RFL6 cells; 3) To explore LO effects on the downregulation of its collagen and elastin substrates and on the elastin repair in CdR-RFL6 cells; and 4) To demonstrate elevation of cellular MT and GSH, perturbation of Cu homeostasis and downregulation of LO as key mechanisms in **emphysema** pathogenesis of rats receiving Cd by chronic administration. The outcome of the proposed research is expected to define key aspects of Cd modulation of LO gene expression and processing by perturbation of Cu homeostasis in the lung, thus enhancing our understanding of the molecular mechanisms for Cd **emphysema** pathogenesis.

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

- **Project Title: LUNGS PATHOLOGY DETECTION USING HYPERPOLARIZED 129XE**

  Principal Investigator & Institution: Ruppert, Kai; Director of Research; Advanced Mri Technology, Llc 652 Petaluma Ave, Ste J Sebastopol, Ca 95472

  Timing: Fiscal Year 2003; Project Start 17-SEP-2003; Project End 31-AUG-2007

  Summary: (provided by applicant): The development of novel hyperpolarized 129Xe nuclear magnetic resonance (NMR) techniques is proposed to non-invasively assess global and regional lung function as well as physiology in-vivo, without the use of radioactive substances or ionizing radiation. It is hypothesized that xenon uptake and exchange dynamics can be reliably detected and exploited to provide pulmonological information that is unobtainable with any other diagnostic modality. In an optimized form these new techniques are expected to become a powerful addition to the arsenal of pulmunologists since they may permit the early detection of pathological changes in the lung parenchyma as well as the study of disease progression and the monitoring of treatment. Once the technologies have been developed they will be tested on an **emphysema** disease model in rabbits to evaluate whether they provide substantial advantages in the early diagnosis of COPD over existing methods. Although a suggested application is the detection of emphysematous lung the investigated methods will help characterize lung function and increase the sensitivity for lung pathology in general. These goals will be approached in three stages. First, using a series of frequency-selective RF pulses centered at the resonance for 129Xe dissolved in the lung parenchyma the uptake and exchange parameters in rabbits and dogs will be determined. The obtained parameter values are used to optimize xenon-polarization-transfer-contrast magnetic resonance imaging sequences, which can be sensitized to map the surface-to-volume ratio or the lung tissue density. In a second step, the methods will be further refined to distinguish gas exchange between alveoli and tissue from exchange between alveoli and red blood cells. Finally, the performance of the optimized NMR pulse sequence techniques will be evaluated by detecting and monitoring the development of **emphysema** in a rabbit model.

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

- **Project Title: MECHANISM BASED INHIBITORS OF SERINE PROTEINASES**

  Principal Investigator & Institution: Groutas, William C.; Distinguished Professor; Chemistry; Wichita State University Wichita, Ks 67208

  Timing: Fiscal Year 2001; Project Start 10-DEC-1997; Project End 30-NOV-2001

  Summary: An array of inflammatory diseases such as pulmonary **emphysema,** chronic bronchitis, cystic fibrosis, psoriasis, rheumatoid arthritis and others, are characterized by an influx of neutrophils, and the presence of mediators of inflammation and cytokines that serve as neutrophil chemoattractants. The recruitment and degranulation of neutrophils in inflammatory states results in the production of reactive oxygen species and the extracellular release of the serine proteinases elastase, cathepsin G and proteinase 3. Poor regulation of the activity of these enzymes because of depressed levels of their physiological protein inhibitors leads to the degradation of the major components of the extracellular matrix and, ultimately the onset of disease. The use of innovative strategies that seek to counteract the damaging effects of the renegade enzymes be reestablishing a proteinase/antiproteinase inhibitor balance constitutes the long-term objective of the proposed research. The use of a potentially universal heterocyclic scaffold in the design of mechanism-based inhibitors that endows these inhibitors with unique mechanistic features and optimal biochemical properties is proposed.

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

- **Project Title: MECHANISMS OF CYTOPROTECTION IN ACUTE LUNG INJURY**

  Principal Investigator & Institution: Choi, Augustine M.; Professor; Medicine; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

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

  Summary: (provided by applicant): The lung is a major target organ for oxidant injury. Damaging effects of reactive oxygen species (ROS) including superoxide and hydroxyl radicals, and hydrogen peroxide, are generated by the incomplete reduction of oxygen. These toxic ROS can damage cellular constituents such as nucleic acids, proteins, and lipids and play a vital role in both acute and chronic inflammatory diseases of the lung such as adult respiratory distress syndrome (ARDS), pulmonary fibrosis, asthma and **emphysema.** It is now apparent that the expression of a variety of genes are regulated following oxidant lung injury, and some of these gene products such as the gaseous molecules carbon monoxide (CO), nitric oxide (NO), and the growth factor keratinocyte growth factor (KGF), and the antioxidant enzyme extracellular superoxide dismutase (ECSOD) are cytoprotective against oxidant lung injury. It is a unifying hypothesis of this program project that these various cytoprotective molecules mediate their effector protective functions via distinct and overlapping signal transduction pathways. We will test this hypothesis by addressing these aims: 1) We will examine the mechanism by which CO mediates cytoprotection against hyperoxia, in particular the role of p38 MAPK in mediating CO-induced cytoprotection. 2) We will focus on the mechanism by which KGF-induced activation provides survival signaling in response to oxidant lung injury. 3) We will focus on the anti-apoptotic effects of iNOS derived NO in limiting injury to the pulmonary endothelium of intact mice exposed to 100% oxygen and the mechanism by which NO inhibits LPS-induced apoptosis in cultured mouse lung endothelium (MLEC). 4) We will examine the mechanism by which EC-SOD in the lung defend against oxidant-induced lung injury. These proposed studies will provide novel

insight into oxidative and signaling mechanisms that contribute to acute lung injury and point to potential new therapeutic targets.

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

- **Project Title: MESENCHYMAL STEM CELL THERAPY: A1 ANTITRYPSIN DEFICIENCY**

  Principal Investigator & Institution: Verfaillie, Catherine M.; Professor; Medicine; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

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

  Summary: (provided by applicant): Alpha-l-antitrypsin (alpha1AT) is a plasma protein, produced in the liver that inhibits elastase, alpha1AT-deficiency is an autosomal recessive disorder that affects approximately 105 individuals in the US. Liver injury in alpha1AT-deficiency is caused by the hepatotoxic effects of mutant alpha1AT retained within the endoplasmic reticulum (ER) of hepatocytes, and **emphysema** by uninhibited proteolytic damage to elastic tissue in the lung parenchyma. Orthoptic liver transplantation is the only curative therapy for alpha1AT-mediated liver disease. If a reliable source of hepatocytes were available, they could conceivably be used to replace 20-25% of the host liver, elevating plasma levels of alpha1AT to greater than 10 muM, and preventing pulmonary toxicity due to alpha1AT-deficiency. We have identified multipotent adult progenitor cells, or MAPC, that can be cultured from human, mouse and rat bone marrow (BM). Single MAPC differentiate into mesodermal, neuroectoderm-like cells and functioning hepatocyte-like cells in vitro. MAPC do not form tumors when infused IV, IM or SQ, but differentiate in response to local cues into hematopoietic cells and epithelium of lung, intestine and liver. For MAPC derived hepatocytes to be suitable for therapy of alpha1AT, or other liver disorders, better characterization of the in vitro differentiation process will be needed. In addition, we will need to demonstrate that MAPC-derived cells function like hepatocytes in vivo. We propose three aims to determine whether MAPC-derived hepatocytes may be a source of cells to treat alpha1AT-deficiency mediated pulmonary and/or liver disease. Studies in SA1 will further demonstrate that hepatocyte like cells can be generated from bone marrow derived MAPC, and develop methods to select progenitors/precursors for hepatocytes generated during culture. Selection of such progenitors will serve two purposes: characterization of differentiation from pluripotent adult stem cells to hepatocytes, and generation of a potential source of cells for effective transplantation in liver disease. Studies described in SA2 that will assess all functions of mature hepatocytes in spheroid cultures should help confirm that hepatocytes generated from BM MAPC are similar to hepatocytes derived from primary liver. Studies in SA3 will establish whether MAPC themselves, MAPC-derived hepatocyte progenitors or mature hepatocytes can restore liver function in vivo, in the setting of hepatocyte cell death and in the setting of abnormal liver function but without liver cell death. This should lay the groundwork for future studies testing whether MAPC or MAPC-derived hepatocyte progenitors/hepatocytes can serve as a suitable source of cells for therapy of alpha1AT, a single gene defect associated with lung damage and/or liver failure.

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

- **Project Title: METALLOELASTASE INDUCTION FOLLOWING INTEGRIN KNOCKOUT**

  Principal Investigator & Institution: Morris, David G.; Medicine; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

Timing: Fiscal Year 2001; Project Start 08-FEB-2001; Project End 31-JAN-2006

Summary: (Adapted from applicant?s abstract) Dr. David Morris is a pulmonary and critical care physician with a strong commitment to an academic career as an independent investigator in respiratory cellular and molecular biology. His particular interest is lung remodeling. Through work in the Lung Biology Center at UCSF/SFGH he has identified a novel animal model of bronchitis and **emphysema** resulting from inactivation of an epithelial integrin (alpha2- beta6). He is proposing a program of advanced research training consisting of independent experimental studies mentored by an expert in integrin biology (Dr. Dean Sheppard); a research advisory committee including experts on matrix metalloproteinases (Dr. Zena Werb), protease biology (Dr. Caughey), and pulmonary immunology (Dr. Erle); and a formal didactic program including courses in biochemistry, cell biology, and immunology. His research program will address the hypothesis that the integrin alpha2-beta6 on the surface of respiratory epithelial cells modulates alveolar macrophage expression of Macrophage Metalloelastase (MME, MMP-12) thereby regulating airway inflammation, and matrix degradation. He will address this hypothesis through three specific aims. First, he will determine which regions of the beta6 integrin subunit are critical to prevent persistent MMP-12 (MME) overexpression by alveolar macrophages and avert the development of **emphysema** in beta6 -/- mice using novel transgenic lines. Second, he will determine the role of MMP-12 (MME) upregulation in the recruitment and activation of macrophages and lymphocytes in beta6 -/- mice using double knockout mice. Finally, he will determine the role of Transforming Growth Factor Beta1, and of alpha2-beta6 mediated activation of latent TGFbeta1 in the regulation of airway inflammation and MMP-12 (MME) expression in vivo using both adenovector gene transfer and transgenic approaches. This work promises to yield important insights into the fundamental biology underlying both chronic airway inflammation and **emphysema.** Dr. Morris will complete this work in the Lung Biology Center (LBC), internationally recognized research center with an outstanding record of training independent academic pulmonary scientists. The Department of Medicine and LBC are fully committed to Dr. Morris? career development and to making all necessary resources available to facilitate successful completion of this work.

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

- **Project Title: MOLECULAR MECHANISMS OF LUNG BRANCHING MORPHOGENESIS**

  Principal Investigator & Institution: Shi, Wei; Children's Hospital Los Angeles 4650 Sunset Blvd Los Angeles, Ca 90027

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

  Summary: Early embryonic lung development, particularly early branching morphogenesis, is controlled by epithelium-mesenchyme interaction, in which autocrine/paracrine growth factors, including BMP4, are involved. This proposal is focused on determining the mechanisms by which BMP4 induces lung branching morphogenesis in mouse. Hypothesis: BMP4 induces mouse embryonic lung epithelial branching morphogenesis in a mesenchyme-dependent manner through activation of specific downstream signaling proteins. Specific Aims: Aim 1. To determine mesenchyme mediated inductive mechanisms of BMP4 on epithelial branching morphogenesis of E11.5 mouse embryonic lung. Aim 2. To define gene expression pattern, specific activation, and biological function of specific BMP4 receptors and downstream Smads during BMP4 induced embryonic lung branching morphogenesis. Aim 3. To determine the biological roles of specific negative regulators (Gremlin, NMA,

and Smad6) of BMP4 signaling during embryonic lung branching morphogenesis. Health Relevance: The studies will provide fundamental knowledge about BMP4 and lung development, which will help us to better understand congenital and neonatal pulmonary diseases as well as lung injury repair. This basic information may aid in the future design of novel therapeutic strategies to prevent and treat such serious pulmonary diseases as lung hypoplasia, bronchopulmonary dysplasia and **emphysema.**

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

- **Project Title: MURINE MODELS OF OCCUPATIONAL COPD**

  Principal Investigator & Institution: Leikauf, George.; Professor; Environmental Health; University of Cincinnati 2624 Clifton Ave Cincinnati, Oh 45221

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

  Summary: Chronic obstructive pulmonary disease (COPD) is marked physiologically by airflow limitations and pathologically by mucosal injury and inappropriate repair in the airway (bronchitis) and parenchyema (emphysema). COPD is currently the fourth leading cause of death in the United States and has long been associated with certain occupations. These include mining, chemical manufacturing, farming, food preparation, and farming. A common feature of COPD, airway mucus hypersecretion is due to excessive production of mucins. These proteins provide the characteristic viscosity, adhesiveness, and elasticity to the mucus lining the airways. To date, nine human mucin genes have been identified and partially characterized in lung disease. This study seeks to use a potent aldehyde, acrolein, to induce mucus hypersecretion in a laboratory species. This aldehyde is a member of a chemical class, the low molecular weight aldehydes, that have excessive use in industry and can result in wide industral exposures. Acrolein is also produce by a number of combustion processes and can be found in diesel, wood, and cigarette smoke in high concentrations. The overall hypothesis of this study is that occupational aldehyde exposures can induce mucus hypersecretion by direct and indirect inflammatory mechanisms. Specific aims include: (1) To develop a mouse model for the study of acrolein-induced COPD, (2) To further investigate the role of macrophage/monocyte or neutrophil infiltration in mucus hypersecretion, and (3) To begin to investigate the genetic determinants of individual susceptibility. These aims will be completed using novel research approaches (including normal, transgenic, and knockout mice with deficient or enhanced leukocyte migratory capacities). Genetic analyses will include strain distribution pattern, mode of inheritance, recombinant inbred, and quantitative trai locus analysis. The well-characterized mouse model generated by this proposal will be useful in the further understanding of the relationship between occupational exposures, genetic markers, inflammatory responses, and COPD.

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

- **Project Title: NEUTROPHILS TRANSENDOTHELIAL MIGRATION: MOLECULAR EVENTS**

  Principal Investigator & Institution: Burns, Alan R.; Principal Member of Technical Staff; Medicine; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

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

  Summary: The project's long term goal is to determine the molecular events that regulate neutrophil migration across the vascular endothelium. While neutrophil adhesion to the endothelium involves at least four classes of adhesion molecules, precisely how adhesion molecules regulate neutrophil migration is unknown. In vitro,

greater than 75 percent of neutrophil migration occurs at tricellular corners where the borders of three endothelial cells converge and tight junctions are discontinuous. The two Specific Aims in this proposal are motivated by the working hypothesis that neutrophil migration at these sites is determined by the numbers, types, and spatial distribution of adhesion molecules and chemotactic factors on the endothelial surface. We will use genetically altered mice with targeted deletions of adhesion molecules in two areas of investigation. The first aim will determine in vitro the relative contribution of adhesion mechanisms to neutrophil migration at endothelial tricellular corners using mouse and human models. Specifically, isolated neutrophils and cultured endothelial cells will be used in adhesion assays to examine the functional role of leukocyte (CD11a/CD18 and CD11b/CD18) and endothelial (CD31, CD54, CD62E, CD62P) adhesion molecules and chemotactic factors (IL-8, PAF, MIP-2, and KC) in neutrophil migration at tricellular corners. For comparative purposes, the role of adhesion molecules in neutrophil migration across HUVEC monolayers will be assessed using blocking monoclonal antibodies. The spatial distribution of adhesion molecules and chemotactic factors will be characterized using immunogold scanning electron microscopy. The organization of tight junctions and the three-dimensional pathway taken by the neutrophil as it penetrates the endothelium will be determined by freeze-fracture transmission electron microscopy. The second aim will examine an in vivo model of acute inflammation in the mouse to determine if tricellular corners are preferred migration sites and if they are regulated by specific adhesion mechanisms. Specifically, TNFalpha, formyl peptide, or MIP-2 will be injected intrascrotally to induce neutrophil migration from the cremasteric microvasculature. The role of specific adhesion molecules in defining the migratory pathway will be assessed by light microscopy using silver stained whole mount preparations and by serial section reconstruction using transmission electron microscopy. Whether neutrophil migration affects endothelial tight junction organization will be assessed using freeze-fracture electron microscopy. Collectively, these studies will provide new insights into the molecular mechanisms regulating neutrophil migration across the endothelium. While leukocyte emigration is critical for host defense and normal healing, it is also partly responsible for a number of pathologic disorders (e.g., ischemia-reperfusion injury in the heart, rheumatoid arthritis, asthma, and emphysema). The proposed research will provide new data and insights for the design of anti-inflammatory therapies that target the multistep process of leukocyte migration.

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

- **Project Title: NICOTINE ABUSE /SMOKING-RELATED DISEASE SUSCEPTIBILITY**

  Principal Investigator & Institution: Hoidal, John R.; Chief, Pulmonary Division; University of Utah 200 S University St Salt Lake City, Ut 84112

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

  Summary: (provided by applicant): OBJECTIVE: The goals are to determine how nicotine contributes to the dysregulated inflammation and abnormal repair that leads to chronic obstructive lung disease (COPD), the link of nicotine addiction to COPD and the genetic basis for the development of COPD. HYPOTHESIS: We hypothesize that many of the effects of smoking on the lung including the dysregulated inflammatory response and impaired repair that lead to COPD are mediated, in part, by functional alterations induced following the interaction of nicotine with nicotinic acetylcholine receptors (nAChRs) expressed on leukocytes or resident lung cells. We also hypothesize that polymorphisms in nAChRs couple with other common gene-based polymorphisms to

increase susceptibility to COPD. SPECIFIC AIMS: The first aim will characterize nAChR expression on leukocytes and selected resident lung cells, and will determine the relationship between receptor expression and cell function. It will test the hypothesis that nicotine's ability to induce inflammation and inhibit repair are dependent on the pattern of nAChR expression on leukocytes and resident lung cells. The second aim will correlate patterns of nAChR expression in inbred mouse strains to susceptibility to COPD. It will test the hypothesis that susceptibility to **emphysema** in mice is determined by the pattern of nAChR expression. The third aim will determine the relationship between nicotine receptor expression and lung function decline in cigarette smokers. It will test the hypothesis that the pattern of leukocyte nAChR expression predicts lung function decline in COPD subjects. The fourth aim will identify genetic factors that play a role in the development of COPD, focusing, in particular, on the relationships between the genetics of nicotine addiction and those of COPD. It will test the hypothesis that polymorphisms in nAChR couple with other common gene-based polymorphisms to increase susceptibility to COPD.

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

- **Project Title: NMR IMAGING OF INERT FLUORINATED GASES IN LUNGS**

  Principal Investigator & Institution: Kuethe, Dean O.; Scientist; New Mexico Resonance 2301 Yale Blvd Se, Ste C1 Albuquerque, Nm 87106

  Timing: Fiscal Year 2002; Project Start 01-APR-1997; Project End 31-JUL-2005

  Summary: (provided by applicant): This project endeavors to provide safe non-invasive, but powerful imaging methods for studying pulmonary physiology and diagnosing and evaluating lung diseases. One aim is to develop a new method of imaging alveolar ventilation to blood perfusion ratios (VA/Qs). The spatial distribution of this ratio is of central diagnostic importance in obstructive lung disease and characterizes the lung's ability to exchange gas. An advantage of our new method over our prior one is that patients who regularly breath oxygen enriched air will not have to breath gas with normal oxygen concentrations, but can breath a mixture rich in oxygen the entire time. The method will be developed in laboratory rats. Specifically, it involves imaging the longitudinal nuclear magnetic relaxation time of an inert fluorinated gas, which we recently discovered is a monotonic function of VA/Q. Because it will quantify VA/Qs in the low range that cause poor arterial blood gases, it is not only potentially a diagnostic tool but also a tool for advancing the physiology of gas exchange in diseased and normal individuals. After development, both VA/Q imaging methods will be applied to a study of elastase induced **emphysema** in rats. A second aim is to systematically develop methods to detect magnetic particles in images of inert fluorinated gas. The methods will be applied to collaborative studies of the patterns of deposition of magnetically labeled aerosol particles in rat lungs and the invasion of transplanted rat lungs by magnetically labeled immune cells. Understanding of how and where aerosol particles deposit in lungs is important to advancing the toxicology of inhaled air pollution and can further the effectiveness of inhaled drugs. Imaging lung rejection is important to diagnosing acute rejection and studying the rejection process to develop improved immunosuppressive strategies. Specifically, we will tailor methods of detecting magnetic particles in gas images for use in our collaborator's animal models and laboratories by systematic exploitation of the frequency shift and diffusional signal loss contrast mechanisms. With this second aim, we will advance inert fluorinated gas imaging beyond a development and demonstration stage to a new research tool that provides previously unavailable data to medical research.

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

- **Project Title: NOVEL PAI-1 INHIBITORS OF NEUTROPHIL PROTEINASES**

  Principal Investigator & Institution: Day, Duane E.; Molecular Innovations, Inc. 21315 Hilltop St Southfield, Mi 48304

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

  Summary: (provided by applicant): This proposal aims to examine the feasibility of using plasminogen activator inhibitor type 1 (PaI-i) mutants as inhibitors of the neutrophil proteinases, neutrophil elastase and cathepsin G. Native PAI-i is not an inhibitor of neutrophil enzymes but preliminary studies presented in this grant show that its specificity can be readily changed by site directed mutagenesis. Apart from inhibiting neutrophil proteinases, other properties of PAI-i make it an attractive candidate for a therapeutic for pathologies involving tissue destruction by neutrophil proteinases. Unlike the endogenous inhibitors of neutrophil proteinases, PAI-i is an effective inhibitor of surface bound proteinases. In addition, PAI-i in complex with proteinases is cleared by receptor-mediated endocytosis more efficiently than the endogenous inhibitors. Our colleagues at the Holland Laboratories of the American Red Cross demonstrate that a single amino acid mutation in reactive center bond of PAI-i converts it to an effective inhibitor of pancreatic elastase without affecting receptor-mediated endocytosis. Based on these findings we propose to design and produce specific PAI-i mutants that inhibit the neutrophil elastase and cathepsin G. PROPOSED COMMERCIAL APPLICATIONS: Pulmonary diseases, such as those caused by cigarette smoke and genetic deficiency are associated with serious tissue damage caused by the proteinases neutrophil elastase and cathepsin G. A current therapy for hereditary **emphysema** (deficiency of alpha one proteinase inhibitor) is replacement with fractions of human plasma containing the missing inhibitor. The current treatment is of limited availability. There are more than 100,000 hereditary **emphysema** sufferers in the US alone. Development PAI-1 mutants targeted to neutrophil elastase and cathepsin G provide a strong commercialization potential for a superior alternative to current therapies treating **emphysema** and offer the hope of treating other inflammatory diseases.

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

- **Project Title: NOVEL SNP-ALLELE GENOTYPING METHOD**

  Principal Investigator & Institution: Peltz, Gary A.; Assistant Director; Syntex (Usa), Inc.-Research Division 3401 Hillview Ave Palo Alto, Ca 94304

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

  Summary: 1. Develop an efficient, low cost SNP genotyping system for experimental murine intercrosses. - A database for computational selection of genotyping primers will be established. Assays for 200 SNPs, with a known chromosomal location will be produced, and alleles in 10 inbred murine strains and two different mouse species will be characterized. - Two experimental murine intercross populations will be genotyped by this method. 2. Demonstrate that this method can accurately determine allele frequencies in pooled murine DNA samples, which will greatly accelerate complex train analysis in murine genetic models of human disease. DNA samples from phenotypically extreme F2 progeny (top or bottom 10%) will be pooled to form two groups, and genotyped to rapidly identify chromosomal regions regulating susceptibility to **emphysema** and polycystic kidney disease. 3. The accuracy and reproducibility of this method for pooled human DNA samples will be determined. To identify cardiovascular disease susceptibility genes, DNA samples from 1000 probands and 1000 case controls have been individually genotyped at 35 SNPs in 16 genes. The samples will be pooled

into disease affected and control groups and allele frequencies in the pooled samples will be measured and compared to the results from genotyping individual samples. - The statistical significance of the measured differences, and the sensitivity of screening studies of this type to detect disease-associated polymorphisms will be assessed.

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

- **Project Title: PATHOBIOGENESIS OF HERITABLE PULMONARY EMPHYSEMA**

  Principal Investigator & Institution: Sifers, Richard; Pathology; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2001; Project Start 01-FEB-2000; Project End 31-JAN-2004

  Summary: Posttranslational elimination of incorrectly folded polypeptides from the endoplasmic reticulum ensures that only functional proteins are deployed to dista1 compartments of the secretory pathway. It is now recognized that by "silencing" the posttranslational expression of mutant gene products, conformation-based quality control functions as a common basis for a diverse set of heritable pathologic conditions, each of which is caused by the hindered intracellular transport of a distinct mutant protein. Chronic destruction of lung connective tissue, resulting from heritable plasma alpha1-antitrypsin (AAT) deficiency, is caused by the impaired secretion of incompletely folded genetic variants of the protein from liver hepatocytes. The long-term goal of this research program is to gain molecular insight into the conformation-based quality control of AAT secretion. To this end, it is now understood that the processing of asparagine-linked oligosaccharides can facilitate the folding of a polypeptide to which they are attached by promoting a physical interaction with lectin-like molecular chaperones of the endoplasmic reticulum. Recent evidence indicates that the removal of mannose from asparagine- linked oligosaccharides functions as an obligatory step in the intracellular disposal of misfolded AAT, indicating that an overlap may exist between protein folding and degradation machinery. The hypothesis to be tested is that modification by intracellular mannosidases sorts genetic variant PIZ for non-proteasomal elimination by promoting specific sequential interactions with the glycoprotein folding sensor UDP- glucose:glycoprotein glucosyltransferase and a novel 95 kDa phosphorylated protein. Metabolic radiolabeling, coimmunoprecipitation of protein complexes, glycosidase inhibition, protein purification from transgenic mouse liver, and molecular cloning will be employed in three specific aims which are to: (1) elucidate how modification by intracellular mannosidases generates a nonproteasomal "degradation signal", (2) determine whether reversible phosphorylation of a novel 95 kDa protein (pp95) regulates its physical interaction with variant PI Z, and (3) characterize pp95 and elucidate its obligatory role in PI Z disposal through the molecular cloning and expression of the recombinant molecule. Results from this study will identify the combinatorial roles of protein folding and quality control machinery in heritable plasma AAT deficiency plus enhance our understanding of how these fundamental processes participate in normal cell physiology.

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

- **Project Title: PORTABLE CONTINUOUS OXYGEN SYSTEM**

  Principal Investigator & Institution: Appel, W Scot.; Sequal Technologies, Inc. 11436 Sorrento Valley Rd San Diego, Ca 92121

  Timing: Fiscal Year 2003; Project Start 04-AUG-2003; Project End 31-JAN-2004

  Summary: (provided by applicant): Chronic obstructive pulmonary disease (COPD) is a serious public health problem that is responsible for more than 500,000 hospitalizations,

100,000 deaths, and $15 billion in direct costs of medical care in the U.S. each year. In addition, millions of Americans are disabled by lung disease. It is estimated that more than 16 million people have undiagnosed COPD. Patients, whom have developed **emphysema** or obstructive bronchitis or who are afflicted with long-standing, low, blood-oxygen levels (chronic hypoxemia), typically require supplemental oxygen. Oxygen concentrators--electrically powered mechanical devices that extract oxygen from air by a process known as Pressure Swing Adsorption (PSA)--are the most prevalent devices used to provide supplemental oxygen (0.5 - 3.0 liters per minute). When low-flow supplemental oxygen is prescribed for the treatment of COPD or chronic hypoxemia, a patient is provided with a stationary oxygen concentrator for use in their home, plus several small tanks of gaseous oxygen and accessories (an oxygen conserving device & pressure regulator) for ambulation or excursions outside their home, including airline travel. SeQual Technologies has developed an advanced PSA gas separation system for the generation of oxygen for medical applications. This proprietary system incorporates a rapid vacuum-pressure-swing adsorption process that enables SeQual to provide a PSA unit with both the highest recovery (the ratio of output oxygen molecules to input oxygen molecules) and the greatest productivity (the oxygen output flow rate per unit volume of the system) of any medical oxygen concentrator. The Company's proprietary PSA devices--in combination with state-of-the-art, high efficiency, lightweight motors and compressors--have enabled SeQual to produce a unique, portable, battery-operated, oxygen concentrator system. SeQual's continued efforts remain in the improvement of the efficiency, productivity and recovery of oxygen molecules during the PSA process to effectively miniaturize the oxygen generation device that will lead to a very small scale portable oxygen concentrator that can deliver continuous oxygen to a patient at all times. The focus of this research is on novel monolithic structured adsorbents. The study proposes to characterize the surface area of the structures, study the effectiveness of the unique pressure swing adsorption cycles and parameters and design a very small system for the concentration of oxygen.

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

- **Project Title: POSTTRANSCRIPTIONAL REGULATION OF TROPOELASTIN EXPRESSIO**

  Principal Investigator & Institution: Parks, William C.; Associate Professor; Pediatrics; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

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

  Summary: Resiliency in lung and arteries is provided by an extracellular matrix that is rich in elastic fibers. Elastin, the principal component of elastic fibers, is the product of crosslinked tropoelastin monomers. The production of elastin is unique among connective tissue proteins in that expression is limited to a brief period of development. By maturity, assembly of elastic fibers is complete, and synthesis of tropoelastin has ceased. However, certain diseases, such as pulmonary hypertension and **emphysema,** are associated with an abnormal or continued accumulation of elastin. To understand the mechanism of such aberrant production, the normal regulation of tropoelastin expression needs to be delineated; however, only minimal information is currently available on the molecular control of elastogenesis. The preliminary data for this grant indicate that downregulation of tropoelastin expression is primarily controlled posttranscriptionally, and the work proposed here focuses on a detailed, molecular characterization of this unique mechanism. This grant will test the hypotheses that the normal cessation of elastogenesis is controlled by an accelerated decay of tropoelastin

mRNA and that specific sequences in the transcript are involved in this regulatory mechanism. For these studies, the generality of this mechanism will be determined by assessing the regulation of tropoelastin production under different conditions, such as hormone treatment, time in culture and age of the cell donor, and with models of in vivo elastin production during development. The effect on tropoelastin transcription, which is expected to be minimal, will be assessed by nuclear run-off assay, by reverse transcription/polymerase chain amplification of tropoelastin pre-mRNA and by transfection with tropoelastin promoter-plasmid constructs. Since transcript turn over can be affected by diverse pathways, a detailed characterization of the accelerated degradation of tropoelastin mRNA will be performed by different methods. Specific enzymatic decay of tropoelastin mRNA will be examined to determine if such mechanisms are activated in response to inhibitors of elastin production. A nuclease protection assay will be used to determine if the status of polyadenylation correlates with the turn over of tropoelastin mRNA, and regulatory sequences in the mRNA will be identified by monitoring the response of reporter constructs containing defined sequences coding for tropoelastin mRNA to downregulation of tropoelastin expression. The interaction of these and other sequences with cellular factors will be determined by gel retardation assay using synthetic fragments of tropoelastin mRNA. Information from these studies will provide new and valuable information on the control of elastogenesis and will lead to the eventual characterization of specific cellular factors that are involved in the regulation of elastin production in development and disease.

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

- **Project Title: PROTEOLYTIC ENZYMES AND INHIBITORS IN LUNG DISEASE**

  Principal Investigator & Institution: Travis, James; Professor; Biochem and Molecular Biology; University of Georgia 617 Boyd, Gsrc Athens, Ga 306027411

  Timing: Fiscal Year 2001; Project Start 01-JAN-1982; Project End 31-MAR-2002

  Summary: The primary goals of the current proposal involve a continuation of investigations designed to determine both the role of host and non-host proteinases in the development of lung-associated diseases as well as the mechanisms utilized to protect this organ against uncontrolled proteolytic events. In this context, the specific aims of the grant will involve a) detailed studies of the proteinases from mast cells, neutrophils, pollen, and bacteria which may be involved in the dysregulation of bronchial homeostasis through either the release of bradykinin and/or the degradation of vasoactive peptides, b) examination of the role of cytokines in the increased expression of proteinase inhibitors from hepatocytes, epithelial cells, and astrocytes during the acute phase proteinase response to inflammation, c) determination of the mechanism of interactions of proteinase inhibitors (serpins) with host serine proteinases, and d) analysis of the structure of the tetramer/heparin complex required to form active, stable mast cell tryptase. All of these results should provide significant information as to the role(s) of host and non-host proteinases in the development of allergies, asthma, bronchitis, and **emphysema.** In addition, a clearer understanding of the mechanisms for both increased proteinase inhibitor synthesis and regulation of host proteinases should be forthcoming.

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

- **Project Title: QUANTITATION OF LUNG VENTILATION AND STRUCTURE BY 3HE MR**

  Principal Investigator & Institution: Yablonskiy, Dmitriy A.; Professor; Radiology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

Timing: Fiscal Year 2003; Project Start 15-DEC-2002; Project End 30-NOV-2007

Summary: (provided by applicant): **Emphysema** is a major medical problem in the US and worldwide. Diagnostic methods for the evaluation of **emphysema** should be sensitive to regional lung structure at the alveolar level. Diffusion MRI with hyperpolarized 3He gas that evaluates the 3He-gas ADC (apparent diffusion coefficient) can provide this sensitivity. It offers information on lung microstructure and function not provided by traditional imaging modalities and pulmonary function tests. With 3He diffusion MRI, alveolar size and the integrity of alveolar walls can be evaluated, even though the alveoli are too small to be resolved by direct imaging. This points to the large potential for clinical application of ADC measurements with hyperpolarized 3He gas. However, until recently it was not clear what specific features of lung structure are probed by 3He gas ADC measurements. Recently we proposed a theoretical model based on a large body of histology data that provides this explanation. However, substantial questions must be answered if we are to understand the 3He ADC measurement and optimally exploit its diagnostic potential. In this proposal we will extend our mathematical model that relates anisotropic ADC measurements in lung to lung microstructural parameters. The mathematical model is based on a realistic structure of lung at the acinar level described in terms of acinar airways covered with alveolar sleeves. The theory of gas diffusion in lung is based on our key concept of anisotropic diffusion in lung acinar airways. We will conduct sophisticated multi-dimensional MR experiments on sacrificed mice with healthy lungs to test the fundamental feature of our mathematical model, the anisotropy of ADC. We will develop further and test our new diffusion 3He MRI technique for tomographic "lung biopsy" on a canine model of **emphysema** with physiology similar to human and establish a quantitative relationship between the severity of **emphysema** as determined by CT and the 3He anisotropic diffusivities. We will use 3He diffusion and ventilation MRI together with CT to study normal human subjects and patients with **emphysema.** Inter-comparison of these three techniques will establish quantitative relationships between CT, lung ventilation and anisotropic ADC measurements and will open up possibilities for new interpretations of results obtained by each modality. The potential implications are significant. A comprehensive clinical picture of **emphysema** progression, from initial onset of the alveolar deformation to the final stage, characterized by dramatic loss of lung function, will be established. New methods will be sensitive enough to allow early diagnosis of **emphysema** that will improve patient treatment.

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

- **Project Title: R21 PROJECT--EFFICACY OF OSTEOPATHIC MANIPULATION IN COP**

  Principal Investigator & Institution: Noll, Donald R.; Chairman; Internal Medicine; Kirksville College of Osteopathic Med 800 W Jefferson St Kirksville, Mo 63501

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

  Summary: (APPLICANT'S ABSTRACT): The specific aim for this project is to determine if osteopathic manipulative treatment (OMT) is effective for persons with **emphysema** as a component of their chronic obstructive pulmonary disease (COPD). The major hypotheses to be tested during this research study are: An initial OMT session, designed to improve chest wall compliance and diaphragmatic function, will produce an immediate positive change in pulmonary function parameters and chest wall mobility. OMT sessions over a 12-week period of time will effect sustained improvement in pulmonary function parameters; chest wall mobility as measured by maximum chest

wall expansion and reduction; and other clinical measures such as quality of life, exercise tolerance, and dyspnea. The sham treatment protocol developed will successfully blind subjects to their group assignment while providing an equivalent amount of contact time with the treating physicians relative to the treatment group. Subjects will be randomly assigned to either the OMT treatment or control group. In addition to conventional care for COPD, each group will receive its designated treatment protocol once a week for 13 weeks. The OMT treatment group will receive a standardized OMT protocol, and the control group will receive a standardized sham treatment protocol. Outcome measures will be obtained at baseline; immediately following the first treatment; at 4, 8, and 12 weeks after initiation of treatment; and 4 weeks after termination of the treatment. Outcome variables include pulmonary function tests; quality-of-life questionnaires (including emotional functioning, fatigue, and dyspnea); and measurements of exercise tolerance and chest wall mobility. This research project will be a significant step in expanding the understanding of the role of OMT in the treatment of chronic lung disease. It is expected to yield evidence that OMT is an important adjunctive modality that improves pulmonary function, increases exercise tolerance, relieves dyspnea, and improves quality of life in those with COPD, and that would have widespread clinical application plus significant economic benefits.

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

- **Project Title: REGULATION OF CHEMOKINE MEDIATED LEUKOCYTE FUNCTIONS**

  Principal Investigator & Institution: Richardson, Micheler R.; Associate Professor; Biochemistry; Meharry Medical College 1005-D B Todd Blvd Nashville, Tn 37208

  Timing: Fiscal Year 2002; Project Start 01-JUN-1996; Project End 31-JAN-2007

  Summary: (provided by the applicant): Chemokines are inflammatory mediators of the chemotactic and cytotoxic functions of a large variety of cells including neutrophils, monocytes, eosinophils, basophils and lymphocytes. These functions are initiated through interaction with specific cell surface G-protein coupled receptors (GPCRs). Most chemokines activate more than one receptor on leukocytes. The hypothesis that underlies this application is that since multiple chemokines are present at sites of inflammation, the chemokine receptors activities must be tightly regulated to prevent tissue damage. We have developed a cellular model, a rat basophilic leukemia cell line (RBL-2H3), in which chemokine receptors can be singly or multiply expressed to display many leukocytes activities. These studies have provided striking evidence that these receptors cross-regulate each other?s function at multiple steps. Signal duration and protein kinase C (PKC) activation have been shown to be critical for receptor cross-regulation. Studies in phagocytes and mouse models of peritoneal and skin inflammation have shown a complexity of cross-regulation among interleukin-8 (IL-8) and RANTES. This complexity likely reflects the ability of these chemokines to activate multiple receptors in leukocytes. The overall objective of this application is to elucidate the mechanism(s) of cross-regulation among the receptors for IL-8 (CXCR1 and CXCR2) and RANTES (CCR1 and CCR5) and to identify specific molecular targets in the signaling pathways, which modulate their ability to mediate and undergo cross-desensitization. Mechanisms of cross-desensitization will be investigated by determining the role of different protein kinase C (PKC) isozymes in receptor cross-phosphorylation. The hypothesis that arrestin-mediated receptor internalization modulate signal duration will also be tested in beta arrestin deficient mice. Chemokines are involved in many acute and chronic inflammatory diseases such as rheumatoid arthritis, **emphysema,** cystic fibrosis, chronic bronchitis and bronchiectasis and

proliferation of tumor malignant melanoma cells. Understanding the molecular mechanisms governing the regulation of chemokine will aid in understanding the control of inflammation as well as the etiology of many inflammatory disorders. These studies will also identify specific targets for the development of therapeutic drugs for the modulation of inflammation.

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

- **Project Title: REGULATION OF PULMONARY ELASTIN PRODUCTION BY RETINOIDS**

  Principal Investigator & Institution: Mcgowan, Stephen E.; Associate Professor; Internal Medicine; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2000; Project Start 01-SEP-1997; Project End 31-AUG-2004

  Summary: Destructive inflammatory lung diseases lung diseases such as **emphysema** and bronchiectasis can irreversibly alter the elastic properties of the lung by degradation of the structural protein elastin. Since virtually all of the elastin in the normal lung is produced during early like, studying the factors which regulate elastin synthesis and deposition, and to ultimately repair the elastin network that is damaged in disease. Hypothesis: The perinatal lung contains a supply of retinoids, that it may use during the period of maximal alveolar septal elastin synthesis. Retinoids, and in particular retinoic acid (RA), may promote elastin synthesis by interstitial lung fibroblasts (LIF) and modulate the increase in elastin synthesis that is required for normal alveolar septal formation. Preliminary studies show that the quantities of RA and retinoic acid receptor-gamma mRNA and protein in neonatal rat lung fibroblasts change in a temporal pattern that suggests they could help initiate an increase in elastin synthesis by these cells. Additional studies show that RA increases elastin production by cultured neonatal LIF and acts at the level of transcription. The major goal of the proposed research is to examine the molecular mechanisms by which RA may influence elastin synthesis during normal alveolar development. The acquisition and metabolism of retinoids by lung tissue and isolated LIF will be examined to assess the utilization of endogenous pulmonary stores. The basal and RA- induced expression of the various retinoic acid receptor (RAR) and retinoid-X receptor (RXR) genes will be studied in cultured rat LIF and in LIF isolated from RAR-gamma null mice. RAR and RXR mRNA and protein will be quantitated using ribonuclease protection assays and immunoblotting, respectively. The effects of a dominant negative RAR mutation of elastin expression will be examined in cultured cells. Elastin mRNA, insoluble elastin accumulation, and alveolar growth will be studied in mice bearing gene deletions for RAR-gamma and/or RXR-alpha. The molecular details of the effects of RA on the elastin gene will be elucidated by deletional analysis and mutagenesis of two potential RA response elements (RARE) within the 5' flanking region of the rat elastin gene. Electrophorectic mobility shift assays will be used to demonstrate RA-responsive increases in the binding of nuclear proteins to these elements, in cultured LIF and in the developing lung. A ligation-mediated polymerase chain reaction will be used to evaluate binding of proteins to these putative RARE in the elastin gene in vivo during lung development, and in response to exogenous RA. Elucidation of mechanisms whereby elastin synthesis is initiated in the alveoli would provide novel information that may also be applicable to idiopathic pulmonary fibrosis and bronchopulmonary dysplasia.

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

- **Project Title: REGULATORY ELEMENTS CONTROLLING ELASTIN TRANSCRIPTION**

  Principal Investigator & Institution: Pierce, Richard A.; Associate Professor; Barnes-Jewish Hospital Ms 90-94-212 St. Louis, Mo 63110

  Timing: Fiscal Year 2002; Project Start 15-APR-1995; Project End 30-NOV-2006

  Summary: Elastin is the primary elastic protein in humans, and provides stretch and recoil to lung tissue, blood vessels, and skin. Elastin is primarily synthesized during fetal development and the neonatal period, and is expressed by specific subsets of cells in these tissues. Normally, elastic fibers are among the most durable structures in the body, but destruction of elastic fibers is central to several chronic lung diseases. Elastic fibers in the lungs of very premature infants are not sufficiently developed to withstand the strain of mechanical ventilation, and can be damaged or deposited in clumps, contributing to abnormal lung development. In adults, when lung elastic fibers are damaged or destroyed in diseases such as **emphysema,** there is little effective repair. Consequently, loss of elastic fibers in **emphysema** is central to loss of lung function. Despite a pivotal role in the lung, the mechanisms that control elastin synthesis in a tissue-specific and a developmentally regulated way are still largely unknown. Previous studies found the elastin "promoter" to be weak in transient transfections, and the basis for cell type-specific expression was unknown. In a search for an enhancer-like element that would confer strong activation of the elastin promoter, new studies identified a regulatory region of the elastin gene named T-Exl, found between the start of transcription, and extending into the first exon of the coding region. Inclusion of T-Exl in expression constructs confers cell type-specific expression of elastin in transient transfections, and increases promoter activity in lung myofibroblasts 6-fold. Nuclear extracts from elastin expressing lung myofibroblasts specifically bind this regulatory region in gel shift assays. Further studies have identified the nuclear proteins as members of the SP-1 family of transcription factors. The studies outlined in this proposal will focus on 1) Identifying and delineating the important regulatory sites controlling cell type-specific gene expression using transient transfections with a series of deletion and mutagenized constructs, 2) Characterizing, identifying, and testing the role(s) of transcription factors binding this regulatory region, and 3) Determining the mechanisms that suppress elastin synthesis during chronic inflammation. These approaches will reveal key mechanisms controlling elastin synthesis and identify targets for strategies to modulate elastin synthesis in the lungs of premature infants and in pulmonary **emphysema.**

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

- **Project Title: RESEARCH CORE 2 - ENVIRONMENTAL LUNG DISEASE**

  Principal Investigator & Institution: Tesfaigzi, Yohannes; Staff Scientist; University of New Mexico Albuquerque Controller's Office Albuquerque, Nm 87131

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

  Summary: SUBPROJECT ABSTRACT NOT PROVIDED

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

- **Project Title: RESPIRATORY MECHANICS IN LUNG DISEASE AND SURGERY**

  Principal Investigator & Institution: Loring, Stephen H.; Scientific Director of Respiratory Thera; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

  Timing: Fiscal Year 2001; Project Start 01-AUG-1996; Project End 30-JUN-2006

Summary: (provided by applicant): Chronic obstructive pulmonary disease (COPD) is a life-threatening, debilitating disease affecting more than 2 million Americans. New surgical therapies such as lung transplantation and lung volume reduction surgery (LVRS) can improve quality of life and pulmonary function in COPD. However, questions remain as to which patients are most likely to benefit from these therapies and why surgery is effective in some patients and not in others. We will continue an observational study of respiratory mechanics in a large cohort of patients with COPD before and after lung transplantation and LVRS. Our rationale is that our coordinated program of respiratory mechanical investigation will continue to provide insights and suggest useful measures of respiratory function that will reveal mechanisms of disease. Specific aims are: 1) To measure the maximal inspiratory pressure-volume characteristic of the chest wall in patients before and after lung transplantation or LVRS to assess changes in inspiratory function of the chest wall. We will test the hypothesis that inspiratory function of the chest wall is often compromised after operation, and that chest wall restriction is an important cause of failure to improve after LVRS or single lung transplantation for **emphysema.** If true, this finding would lead to studies of the origins and remedies of chest wall restriction after surgery. 2) To explore the differences between lung volumes measured by multiple breath helium dilution, plethysmography, and computed tomography (CT). Accurate measurements of lung volume are essential for diagnosis, for documentation of hyperinflation, for evaluation of patients before surgery, and for assessment of the effects of LVRS and transplantation. We will test the hypothesis that, contrary to current belief, helium dilution is more accurate than plethysmography in patients with COPD. If true, this finding would change clinical practice in this important group. 3) To develop methods to measure the pressure-area characteristics of the trachea in patients undergoing bronchoscopy and to determine whether the site of expiratory flow limitation in these patients is in the lungs or trachea. Acquired tracheomalacia is reportedly common in patients with COPD, and can cause severe expiratory obstruction that may be relieved by stenting or surgical reinforcement of the airway. We will test the hypothesis that many patients with demonstrated tracheomalacia and central airway collapse have obstruction caused by collapse of intrapulmonary airways, which is not amenable to surgical correction. Our findings will provide normative data on tracheal collapsibility not currently available, explore the association between tracheomalacia and COPD, and test a method for predicting the effect of stenting on expiratory obstruction in these patients.

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

- **Project Title: RESPIRATORY SYSTEM MECHANICS**

  Principal Investigator & Institution: Boriek, Aladin; Assistant Professor of Medicine and Phys; Medicine; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2001; Project Start 01-APR-1991; Project End 31-MAR-2004

  Summary: The respiratory muscles are a major determinant of thoracic cavity shape and thus the distribution of regional ventilation. Respiratory insufficiency is the usual cause of death in many primary neuromuscular disorders. Respiratory muscle fatigue is believed to be a major factor in hypercarbic respiratory failure associated with lung and/or cardiovascular diseases. A recent NHLBI workshop summarized the difficulty of studying respiratory muscle fatigue because of our limited understanding of the relationships between tension developed by the respiratory muscles and pressures which expand the thoracic cavity and other parameters which can be measured in intact animals or man. Much of the benefit of lung volume reduction surgery for end stage **emphysema** is proposed to be secondary to improved function of the respiratory

muscles principally the diaphragm. This project utilizes a video roentgenographic technique to determine the regional shape, displacements and muscle shortening of the diaphragm and rib cage to elucidate the basic mechanics of the diaphragm and rib cage. By comparing muscle shortening and curvature of the diaphragm in intact animals under conditions in which the transdiaphragmatic pressure and muscle tension can be measured, the relationship between muscle tension and pressures can be determined. The detailed three dimensional anatomic data provided by this methodology coupled with more conventional physiologic measurements should answer important questions posed by previous studies of the coupling of the diaphragm abdomen and rib cage. The investigators will verify and extend two models of diaphragm structure and functions developed in the current period of the project. These models are consistent with data obtained in this project which contradict previous qualitative models. The models offer testable predictions about the mechanisms of failure of the diaphragm as an inspiratory muscle at high lung volumes. In the current proposal, the investigators will extend our knowledge and techniques developed in animals to study diaphragm and chest wall function in normal humans and patients with severe **emphysema** before and after lung volume reduction surgery.

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

- **Project Title: RESPONSES TO SURGICAL AND BRONCHOSCOPIC VOLUME REDUCTION**

  Principal Investigator & Institution: Ingenito, Edward P.; Associate Professor; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-MAY-1999; Project End 30-NOV-2006

  Summary: (provided by applicant): Lung volume reduction surgery (LVRS) is an effective adjunct to medical treatment for end stage **emphysema.** Clinical results suggest that LVRS works by eliminating areas of severely diseased and dysfunctional lung. We previously hypothesized that effective volume reduction might be possible using a non-surgical approach to cause permanent atelectasis of specific target regions. By collapsing these regions and applying a fibrin-based sealant, we have shown that it is possible to achieve lung volume reduction without surgery in a sheep model of **emphysema.** While these studies confirmed our initial hypothesis, they have also demonstrated several important shortcomings. BVR achieved solely by mechanical collapse and application of fibrin sealant is frequently incomplete. Only 1/2 to 1/3 of the target regions remained collapsed at 2month follow-up. Furthermore, several target regions developed tissue necrosis. To address these limitations, we have modified our approach to BVR. A new generation of reagents has been developed which modulates local cellular responses, and promotes fibroblast in-growth and scar formation without necrosis. Preliminary studies indicate that these modifications address the limitations identified in our original study. We now hypothesize that: improved BVR can be achieved using washout solution + glue reagents which cause site-specific collapse, and modulation of fibroblast and epithelial cell biology to generate controlled, efficient scar formation. The objectives of this proposal are to: 1) characterize physiological and biological responses using these improved reagents in a sheep model of **emphysema,** and 2) compare results to those obtained using conventional surgical therapy. We believe that by accomplishing these objectives, we can help advance this technology into the clinical arena.

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

- **Project Title: ROLE OF ELASTOLYTIC CATHEPSINS IN EMPHYSEMA**

  Principal Investigator & Institution: Chapman, Harold A.; Professor; Medicine; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

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

  Summary: (Applicant's Abstract): Although excessive proteolysis is a key element in the pathogenesis of **emphysema,** pathways of protease dysregulation in this disorder remain uncertain. New studies implicate lymphocyte-derived cytokines in **emphysema.** Interferon-y acts on macrophages as well as non-inflammatory cells such as smooth muscle cells to promote expression and secretion of the active cysteine protease cathepsin S, a potent elastase stable at neutral pH. Transgenic mice expressing either IL-13 or interferon-y on airway surfaces develop cysteine protease-dependent emphysematous changes. Further, a significant correlation was recently found between serum levels of cystatin C, the major cysteine protease inhibitor, and severe reductions in FEV1 (<20 percent predicted) in a cohort of 30 patients with early-onset **emphysema** compared to controls with normal FEV1 and comparable smoking history. These studies invite the hypothesis that pro-inflammatory cytokines and possibly cigarette smoke stimulate mesenchymal lung cells and macrophages to secrete elastolytic cysteine proteases and downregulate their cystatin C release. This imbalance creates an accelerated process of collagen and elastin degradation important to the development of **emphysema** and COPD. The research plan is centered on the question of whether dysregulation of elastolytic cathepsins is important to the pathogenesis of **emphysema.** Parallel tracks of animal and human experiments are proposed: Mouse cathepsin S/L and cystatin C "knockouts" are used in Aims 1 and 2 to answer the question of whether excess elastolytic cathepsin activity exacerbates the development of interferon-y-induced **emphysema** and whether mesenchymal cells in the lung are a source of these enzymes. Aim 3 is designed to determine if low levels of cystatin C and/or polymorphic markers in or near the major genes regulating cystatin C (and elastolytic cathepsins) are associated with increased risk of COPD. Together, these studies should determine if some patients with early-onset COPD can be grouped, based on either phenotypic (cystatin C) or genetic markers, into a functional subset defined by a common pathogenic pathway involving dysregulation of elastolytic cathepsins.

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

- **Project Title: ROLE OF MECHANICAL FORCES IN THE PROGESSION OF EMPHYSEMA**

  Principal Investigator & Institution: Suki, Bela; Associate Professor; Biomedical Engineering; Boston University Charles River Campus 881 Commonwealth Avenue Boston, Ma 02215

  Timing: Fiscal Year 2002; Project Start 01-DEC-1997; Project End 31-AUG-2005

  Summary: (Applicant's abstract): It is generally accepted that **emphysema** develops through an imbalance of protease and anti-protease activity in the lung, resulting in enzymatic destruction of elastin fibers within the alveolar wall. However, preliminary data from our laboratory demonstrate the **emphysema** can be induced in ways that do not involve elastin. We have observed that collagen fibers in the lung tissue of rats treated only with elastase can rupture under the mechanical forces that are required for normal breathing. Since collagen is much stronger than elastin, and protects the alveoli from rupture at high distending pressures, even if elastin is damaged, the alveolar wall can not possibly rupture unless collagen is weakened, and thus prone to mechanical failure. This observation has led us to formulate two hypotheses: 1) Following the onset

initial progression of **emphysema** due to proteolytic injury, a critical point is reached at which the mechanical forces required to maintain normal breathing are sufficient to gradually damage and rupture the remodeled alveolar walls; 2) A key element of **emphysema** is extracellular repair and the common link among the various animal models of **emphysema** is the generation of remodeled weak collagen fibers that can rupture under mechanical forces. To test these hypotheses we will determine whether mechanical forces can rupture the alveolar walls in three acute injury murine models (elastase, collagenase and proteoglycan digestion treatments) of **emphysema,** and "knock out" and transgenic murine models of spontaneous **emphysema.** Measures of remodeling and inflammation will be correlated with lung function at 2 time points during the progression of **emphysema.** Physiological measurements, biochemical and molecular biology studies as well as simultaneously mechanical failure testing and microstructural imaging will be utilized to: 1) assess whether collagen remodeling is a critical common feature in the pathophysiology of all types of **emphysema;** 2) determine the structural basis for collagen failure; and 3) assess whether the relentless progression of **emphysema** that is observed clinically is due to self-propagating failure that occurs during the process of normal breathing.

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

- **Project Title: SP-D IN PULMONARY REMODELING**

  Principal Investigator & Institution: Korfhagen, Thomas R.; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

  Timing: Fiscal Year 2001; Project Start 01-SEP-1996; Project End 31-JUL-2006

  Summary: (Applicant's Abstract) This application will determine the role of pulmonary surfactant protein D (SP-D) in the modulation of pulmonary inflammation and maintenance of postnatal alveolar structure. SP-D is a member of the collectin family of host defense molecules expressed in various tissues, but at highest levels in the lung where it plays a role in innate immunity. SP-D binds various pathogenic microbes, enhancing phagocytosis, and modulating inflammation. Recently, decreased or absent levels of SP-D were detected in BALF from patients with CF and RSV pneumonia providing a strong inference that decreased SP-D may contribute to lung inflammation. The investigators recently developed mice lacking SP-D by targeted gene inactivation (SP-D -/-) and demonstrated increased pro-inflammatory cytokines and inflammatory cell influx following intranasal or intratracheal instillation of respiratory syncytial virus (RSV) and influenza virus A. SP-D (-/-) mice developed pulmonary inflammation and enlarged alveoli following neonatal RSV infection at 4 days of age. In the absence of RSV, lung development was normal, until 3 weeks of age when SP-D (-/-) mice spontaneously developed pulmonary inflammation and **emphysema,** demonstrating that lack of SP-D contributes to abnormal alveolar remodeling. Thus, the present application will test the central hypothesis that SP-D plays a critical role in modulation of lung inflammation and protection against pulmonary injury following RSV infection of the postnatal developing lung. To test the hypothesis, Aim 1 will determine the role of SP-D in the modulation of RSV induced pulmonary inflammation and airway remodeling in neonatal and postnatal mouse lungs. Aim 2 will determine whether SP-D regulates the balance of proteinases/antiproteinases that the investigators hypothesize underlies the pathogenesis of abnormal alveolar formation in the SP-D (-/-) mice by testing whether SP-D regulates metalloproteinases (NMP) -9, -2, and -12. Aim 3 will determine whether mutations in specific domains of SP-D contribute to or ameliorate neonatal lung inflammation and airway remodeling in mice or in conjunction with the Clinical Core, in infants with chronic lung disease. This SCOR project will clarify the

role of SP-D in modulating pulmonary inflammatory responses and alveolar remodeling and may provide scientific support for the use of SP-D in treatment of chronic lung diseases of children, e.g. bronchopulmonary dysplasia.

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

- **Project Title: STEM CELLS FOR THE PREVENTION AND TREATMENT OF EMPHYSEMA**

  Principal Investigator & Institution: Rennard, Stephen I.; Larson Professor of Medicine; Internal Medicine; University of Nebraska Medical Center Omaha, Ne 681987835

  Timing: Fiscal Year 2003; Project Start 01-AUG-2003; Project End 30-JUN-2007

  Summary: (provided by applicant): This study will evaluate the hypothesis that stem cell/progenitor cell failure leads to inadequate repair of tissue and contributes to the development of **emphysema.** The proposal will also evaluate the related therapeutic implications: by replacing stem cells, the susceptibility of old animals to develop **emphysema** can be mitigated and the repair of the emphysematous lung can be facilitated. Maintenance of lung structure requires adequate, ongoing tissue repair throughout life. Stem/progenitor cell failure could lead to inadequate repair and subsequent net loss of lung tissue, the defining feature of pulmonary **emphysema.** The similarity between senile lung that develops, to some degree, in all aging animals and **emphysema** has been noted and supports this concept. Tissue destruction, for example due to cigarette smoke, is likely to be more disruptive in individuals with inadequate repair. This proposal will determine if pluripotent stem cells can populate the lung and contribute to lung repair. Specifically, the ability of cells derived from old and young animals to repopulate lungs will be assessed using green fluorescent protein (GFP) transgenic mice to provide "marked" stem cells. The ability of these donor cells to repopulate various lung cell compartments will be quantified. The donor cells will be fractionated and characterized using defined cell surface markers. Cells derived from recipient lungs will be assessed for function related to repair in vitro. Finally, the ability of cell transplantation decrease the susceptibility of old animals to develop **emphysema** will be assessed. The ability of stem cell transplantation to facilitate functional and structural repair of the lung in aged and emphysematous animals will be assessed. These studies will establish a role for stem cells in modulating lung repair and provide evidence that use of such cells could play a role in the therapy of destructive lung disorders such as **emphysema.**

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

- **Project Title: T-LYMPHOCYTES, LATENT VIRUS AND EMPHYSEMA PATHOGENESIS**

  Principal Investigator & Institution: Diaz, Philip T.; Associate Professor of Medicine; Internal Medicine; Ohio State University 1800 Cannon Dr, Rm 1210 Columbus, Oh 43210

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

  Summary: (provided by applicant): Recent data has suggested that latent adenoviral infections may up-regulate inflammatory processes in the lung and be an important co-factor in **emphysema** development. In addition recent lung biopsy studies have demonstrated that lung lymphocytes, particularly CD8+ cells are found more commonly in the airway as well as the lung parenchyma in individuals with chronic obstructive pulmonary disease. It has thus been hypothesized that lymphocytes associated with chronic obstructive pulmonary disease represent a cytotoxic T-lymphocyte (CTL) response to latent virus. In support of this hypothesis is data demonstrating a marked

increased susceptibility of HIV infected smokers to **emphysema.** Furthermore, the presence of **emphysema** in this precocious process is associated with increased numbers of cytotoxic lymphocytes on broncho- alveolar lavage. With this as a background, the central hypothesis of the present study is that CTL's represent a response to latent viral infection in the lung and contribute directly to **emphysema** pathogenesis by accelerating apoptotic cell death of lung parenchyma. To address this hypothesis, we examine use lung tissue obtained from subjects enrolled in the National **Emphysema** Treatment Trial undergoing lung volume reduction surgery (LVRS). The specific aims of the current proposal are: Specific Aim 1: To determine the relationship between latent virus infection of lung epithelium, CTL infiltration and programmed cell death in patients with advanced **emphysema.** Specific Aim 2: To determine whether latent viral infection of alveolar epithelium predicts progression of **emphysema** following LVRS. In conclusion, we believe that successful completion of this project will provide us with very important information regarding the role of latent viral infection, upregulation of the inflammatory response and the pathogenesis of **emphysema.**

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

- **Project Title: TRANSGENIC CYTOKINES IN COPD**

  Principal Investigator & Institution: Zheng, Tao; Internal Medicine; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-MAY-2007

  Summary: (provided by applicant): Cigarette smoke (CS) is a major factor in the pathogenesis of COPD. However, only a minority of smokers get COPD and the rate of CS-induced pulmonary deterioration differs greatly amongst individuals. CS induced **emphysema** via altering protease/antiprotease balance in the lung. However, the mechanisms by which CS exerts its effects and the host factors that define individual susceptibility are poorly understood. Inflammation (macrophages, lymphocytes, eosinophils, neutrophils) is common in COPD. The importance of inflammation in generating COPD, the ability of inflammation to alter proteases and antiproteases and, the degree to which different types of inflammation can account for different presentations of patients with COPD have not been defined. We recently established an inducible overexpression (OE) transgenic system and used this system to overexpress IL-13 and/or gamma-interferon (IFN-gamma) in the adult murine lung. Individually both cytokines caused impressive **emphysema.** With IL-13 the **emphysema** occurred rapidly and was associated with mucus metaplasia and macrophage, lymphocyte and eosinophil rich inflammation. In the IFN-gamma mouse, the **emphysema** occurred slowly, was not associated with mucus metaplasia and was associated with macrophage and granulocyte rich inflammation. Mice expressing both IFN-gamma and IL-13 had a synergistic increase in **emphysema.** We hypothesize that: (1) IL-13 and IFN-gamma alone and in combination, activate important **emphysema** generating pathways in the lung; (2) effects of IL-13 and/or IFN-gamma are mediated by distinct and differentiable alterations in pulmonary protease / antiprotease balance and (3) IFN-gamma and IL-13 play an important role in the pathogenesis of CS-induced **emphysema.** To test this hypothesis we propose to: (1) Further define the phenotype and protease / antiprotease alterations in IL-13 OE and IFN-y OE mice and progeny of crosses of these animals. (2) Characterize the importance of IL-13 / IFN-gamma-induced alterations in protease / antiprotease balance in the generation of the **emphysema** seen in these animals. (3) Characterize the expression and roles of IL-13 and/or IFN-gamma in murine CS-induced **emphysema.**

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

- **Project Title: TRANSGENIC MODELING OF COPD**

  Principal Investigator & Institution: Elias, Jack A.; Waldemar Von Zedtwitz Professor of Medic; Internal Medicine; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2001; Project Start 29-SEP-2000; Project End 31-AUG-2004

  Summary: (adapted from the applicants' abstract) Cigarette smoke (CS) is a major factor in the pathogenesis of COPD. However, only a minority of smokers get COPD and the rate of CS-induced pulmonary deterioration differs greatly amongst individuals. CS induces **emphysema** via altering protease/antiprotease balance in the lung. However, the mechanisms by which CS exerts its effects and the host factors that define individual susceptibility are poorly understood. Inflammation (macrophages, lymphocytes, eosinophils, neutrophils) is common in COPD. The importance of inflammation in generating COPD, the ability of inflammation to alter proteases and antiproteases and, the degree to which different types of inflammation can account for different presentations of patients with COPD have not been defined. The investigators recently established an inducible overexpression (OE) transgenic system and used this system to overexpress IL-13 and/or gamma- interferon (IFN-gamma) in the adult murine lung. Individually, both cytokines caused impressive **emphysema.** With IL-13 the **emphysema** occurred rapidly and was associated with mucus metaplasia and macrophage, lymphocyte and eosinophil rich inflammation. In the IFN-gamma mouse, the **emphysema** occurred slowly, was not associated with mucus metaplasia and was associated with macrophage and granulocyte rich inflammation. Mice expressing both IFN-gamma and IL-13 had a synergistic increase in **emphysema.** The investigators hypothesize that: 1) IL-13 and IFN-gamma alone and in combination, activate important **emphysema** generating pathways in the lung; 2) effects of IL-13 and/or IFN-gamma are mediated by distinct and differentiable alterations in pulmonary protease/antiprotease balance; and 3) IFN-gamma and IL-13 play an important role in the pathogenesis of CS-induced **emphysema.** To test this hypothesis, the investigators propose to: 1) further define the phenotype and protease/antiprotease alterations in IL-13 OE and IFN-gamma OE mice and progeny of crosses of these animals; 2) characterize the importance of IL-13/IFN-gamma-induced alterations in protease/antiprotease balance in the generation of the **emphysema** seen in these animals; 3) determine if IL-13 or IFN-gamma alter the production of selected target proteases and/or antiproteases in vitro; 4) determine if the **emphysema** generating effects of IL-13 are restricted to IL-13 or are also a property of IL-4 or other Th2 cytokines; and 5) characterize the expression and roles of IL-13 and/or IFN- gamma in murine CS-induced **emphysema.**

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

- **Project Title: VALIDATION OF FUNCTIONAL LUNG MRI IN PIG MODEL**

  Principal Investigator & Institution: Rizi, Rahim R.; Radiology; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2001; Project Start 15-FEB-2001; Project End 31-JAN-2004

  Summary: (Verbatim from the Applicant's Abstract): Recently, promising new MRI techniques using laser polarized aboutHe and arterial spin tagging (AST) have been developed for studying ventilation and perfusion (V/Q) in human lungs. In patients with **emphysema** and pulmonary emboli (PE), these techniques have produced dramatic images with the characteristic V/Q distributions of these diseases. While preliminary results indicate that this new integrated MRI technique can be used for studying regional V/Q abnormalities, the technique has not been clinically or

physiologically validated. The ultimate clinical usefulness of this non-invasive imaging modality will only be possible if is validated by an established method. The main goal of this proposal is the refinement of V/Q imaging using polarized 3He and AST, and its validation in an animal model. This technique will then aid in the overall assessment of lung function and in the development of a model to quantify ventilation, perfusion, and physiologic V/Q relationships in the normal and diseased lung. We propose to validate 3He/AST method using single-photon emission computed tomography and the multiple inert gas elimination technique by accomplishing the following specific aims: 1. To establish the normal values of the regional helium distribution and perfusion signal in normal pigs. We will perform ventilation with hyperpolarized 3He and perfusion with AST. We will also perform the multiple inert gas elimination technique (MIGET) in each pig to confirm that its V/Q distributions are normal. 2. To obtain 3He ventilation and AST perfusion MRI in pigs after airway occlusion by various sizes of glass beads as an airway model for **emphysema.** 3. To obtain 3He ventilation and AST perfusion MRI in pigs with autologous clot inserted into their pulmonary artery as a model of PE. 4. 3He gas MRI and artenal spin-tagging perfusion scans will be used to deterrnine V/Q changes following the administration of streptokinase as treatment for the induced PE. Once validated, this integrated MRI method will provide novel anatormic and physiologic information for detection and treatment of pulmonary diseases.

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

- **Project Title: VENTING FOR REDUCTION OF HYPERINFLATION IN EMPHYSEMA**

  Principal Investigator & Institution: Cooper, Joel D.; Surgery; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2002; Project Start 01-APR-1999; Project End 31-MAR-2006

  Summary: Description (provided by applicant) **Emphysema** affects approximately 2 million individuals in the US and is the fourth leading cause of death. Once medical therapy has been maximized, further therapeutic strategies are limited, apart from lung transplantation, and lung volume reduction surgery, both of which are applicable to only a small subsegment of end-stage patients. The crippling effects of end-stage **emphysema,** including severe dyspnea, relate not only to loss of lung substance but also to the dynamic hyperinflation of the lungs associated with loss of elastic recoil and a marked increase in the size of the lungs. The concomitant enlargement of the thorax, and flattening of the diaphragm, render the inspiratory muscles inefficient, increase the work of breathing, and contribute significantly to the feeling of breathlessness. The patient is trapped in a state of hyperinflation and no amount of forced effort can empty the lungs since the same force exerted to empty the lungs, is transmitted to the small airways which collapse and obstruct the outflow of gas. There is clear evidence that the normal collateral ventilation present in human lungs is markedly increased in **emphysema** due to extensive breakdown of alveolar walls. In fact, it has been demonstrated that airflow from one region of the lung to another in the emphysematous patient can exceed air flow through the nonnal air passages. We hypothesize that the extensive collateral ventilation existing in emphysematous lungs, can be utilized to decrease the hyperinflation and air trapping which is responsible for a significant portion of the dyspnea in such patients. We propose to create new passageways from the lung substance to large airways in order to bypass the small, obstructed airways. This will allow the lungs to deflate more completely on exhalation, relieving breathlessness and increasing the patients' tolerance for exertion. To accomplish this we propose: 1) to create a dog model of severe **emphysema;** 2) to develop a simple, safe,

and effective endoscopic technique for creation of broncho-pulmonary conduits, using methods applicable for humans; 3) to evaluate the radiologic, physiologic, and functional consequences of alleviating dynamic hyperinflation with this method.

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

- **Acute bilateral emphysematous pyelonephritis successfully managed by medical therapy alone: A case report and review of the literature.** by Flores G, Nellen H, Magana F, Calleja J.; 2002;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=116587
- **Chemical chaperones mediate increased secretion of mutant [alpha]1-antitrypsin ([alpha]1-AT) Z: A potential pharmacological strategy for prevention of liver injury and emphysema in [alpha]1-AT deficiency.** by Burrows JA, Willis LK, Perlmutter DH.; 2000 Feb 15;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=26515
- **Detection of emphysema in rat lungs by using magnetic resonance measurements of 3He diffusion.** by Chen XJ, Hedlund LW, Moller HE, Chawla MS, Maronpot RR, Johnson GA.; 2000 Oct 10;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=17225
- **Increased metalloproteinase activity, oxidant production, and emphysema in surfactant protein D gene-inactivated mice.** by Wert SE, Yoshida M, LeVine AM, Ikegami M, Jones T, Ross GF, Fisher JH, Korfhagen TR, Whitsett JA.; 2000 May 23;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=18543
- **Myosin heavy chain and physiological adaptation of the rat diaphragm in elastase-induced emphysema.** by Kim DK, Zhu J, Kozyak BW, Burkman JM, Rubinstein NA, Lankford EB, Stedman HH, Nguyen T, Levine S, Shrager JB.; 2003;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=150515
- **The role of collagenase in emphysema.** by Foronjy R, D'Armiento J.; 2001;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=64802

---

[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.

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

- **A case of localized persistent interstitial pulmonary emphysema.**
  Author(s): Oh MH, Kim MY, Shim WS, Oh SS, Shin BK, Cho SJ, Kim HK.
  Source: Journal of Korean Medical Science. 2001 April; 16(2): 225-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11306752&dopt=Abstract

- **A case of orbital emphysema associated with internal laryngocele.**
  Author(s): Mensiz E, Tuz M, Oyar O, Dogru H, Yasan H.
  Source: Auris, Nasus, Larynx. 2003 May; 30(2): 197-200. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12753994&dopt=Abstract

- **A new case of alpha-1-antitrypsin frameshift mutation (1123insT) causing severe deficiency and emphysema.**
  Author(s): Feldmann D, Bard M, Chauve C, Couderc R.
  Source: Human Mutation. 2000 November; 16(5): 447.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11058908&dopt=Abstract

- **A novel oral neutrophil elastase inhibitor (ONO-6818) inhibits human neutrophil elastase-induced emphysema in rats.**
  Author(s): Kuraki T, Ishibashi M, Takayama M, Shiraishi M, Yoshida M.
  Source: American Journal of Respiratory and Critical Care Medicine. 2002 August 15; 166(4): 496-500.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12186827&dopt=Abstract

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

- **A pilot study of all-trans-retinoic acid for the treatment of human emphysema.**
  Author(s): Mao JT, Goldin JG, Dermand J, Ibrahim G, Brown MS, Emerick A, McNitt-Gray MF, Gjertson DW, Estrada F, Tashkin DP, Roth MD.
  Source: American Journal of Respiratory and Critical Care Medicine. 2002 March 1; 165(5): 718-23.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11874821&dopt=Abstract

- **A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema.**
  Author(s): Fishman A, Martinez F, Naunheim K, Piantadosi S, Wise R, Ries A, Weinmann G, Wood DE; National Emphysema Treatment Trial Research Group.
  Source: The New England Journal of Medicine. 2003 May 22; 348(21): 2059-73. Epub 2003 May 20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12759479&dopt=Abstract

- **A simple method to save on costs in pulmonary emphysema operations.**
  Author(s): Roviaro G, Varoli F, Vergani C, Maciocco M, Saguatti L.
  Source: The Annals of Thoracic Surgery. 2000 June; 69(6): 1991-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10892981&dopt=Abstract

- **A surgical approach for patients with endstage emphysema.**
  Author(s): Scullion J.
  Source: British Journal of Nursing (Mark Allen Publishing). 1999 September 23-October 13; 8(17): 1129-33. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10897694&dopt=Abstract

- **Acquired lobar emphysema--an unusual cause of respiratory distress.**
  Author(s): V TS, S R HR, Bhatt BV.
  Source: Indian Pediatrics. 2001 April; 38(4): 411-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11313515&dopt=Abstract

- **Acute emphysematous cholecystitis preceded by symptoms of ileus: report of a case.**
  Author(s): Ise N, Andoh H, Furuya T, Sato T, Yasui O, Yoshioka M, Iida M, Takahashi T, Kotanagi H, Koyama K.
  Source: Surgery Today. 2002; 32(2): 183-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11998952&dopt=Abstract

- **Acute emphysematous cholecystitis.**
  Author(s): Van Dyck P, Vanhoenacker P, D'Haenens P.
  Source: Jbr-Btr. 2001 April; 84(2): 77. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11374650&dopt=Abstract

- **Acute fulminant hepatic infection causing fatal "emphysematous hepatitis": case report.**
  Author(s): Blachar A, Federle MP, Brancatelli G.
  Source: Abdominal Imaging. 2002 March-April; 27(2): 188-90.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11847579&dopt=Abstract

- **Advances in thoracic surgery : emphysema and simultaneous bronchial carcinoma.**
  Author(s): Pezzetta E, Fitting JW, Ris HB.
  Source: Swiss Medical Weekly : Official Journal of the Swiss Society of Infectious Diseases, the Swiss Society of Internal Medicine, the Swiss Society of Pneumology. 2003 January 11; 133(1-2): 4-8. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12596089&dopt=Abstract

- **Aerosol morphometry and aerosol bolus dispersion in patients with CT-determined combined pulmonary emphysema and lung fibrosis.**
  Author(s): Kohlhaufl M, Brand P, Scheuch G, Meyer T, Schulz H, Haussinger K, Heyder J.
  Source: Journal of Aerosol Medicine : the Official Journal of the International Society for Aerosols in Medicine. 2000 Summer; 13(2): 117-24.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11010592&dopt=Abstract

- **Airway inflammation in severe chronic obstructive pulmonary disease: relationship with lung function and radiologic emphysema.**
  Author(s): Turato G, Zuin R, Miniati M, Baraldo S, Rea F, Beghe B, Monti S, Formichi B, Boschetto P, Harari S, Papi A, Maestrelli P, Fabbri LM, Saetta M.
  Source: American Journal of Respiratory and Critical Care Medicine. 2002 July 1; 166(1): 105-10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12091179&dopt=Abstract

- **Alpha(1)-antitrypsin deficiency, liver disease and emphysema.**
  Author(s): Parfrey H, Mahadeva R, Lomas DA.
  Source: The International Journal of Biochemistry & Cell Biology. 2003 July; 35(7): 1009-14. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12672469&dopt=Abstract

- **Alpha-1 antitrypsin deficiency in emphysema.**
  Author(s): Khan H, Salman KA, Ahmed S.
  Source: J Assoc Physicians India. 2002 April; 50: 579-82. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12164415&dopt=Abstract

- **alpha-1-Antitrypsin ameliorates cigarette smoke-induced emphysema in the mouse.**
  Author(s): Churg A, Wang RD, Xie C, Wright JL.
  Source: American Journal of Respiratory and Critical Care Medicine. 2003 July 15; 168(2): 199-207. Epub 2003 April 10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12689849&dopt=Abstract

- **Altered glutamate metabolism is associated with reduced muscle glutathione levels in patients with emphysema.**
  Author(s): Engelen MP, Schols AM, Does JD, Deutz NE, Wouters EF.
  Source: American Journal of Respiratory and Critical Care Medicine. 2000 January; 161(1): 98-103.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10619804&dopt=Abstract

- **Alveolar wall apoptosis causes lung destruction and emphysematous changes.**
  Author(s): Aoshiba K, Yokohori N, Nagai A.
  Source: American Journal of Respiratory Cell and Molecular Biology. 2003 May; 28(5): 555-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12707011&dopt=Abstract

- **Amplification of inflammation in emphysema and its association with latent adenoviral infection.**
  Author(s): Retamales I, Elliott WM, Meshi B, Coxson HO, Pare PD, Sciurba FC, Rogers RM, Hayashi S, Hogg JC.
  Source: American Journal of Respiratory and Critical Care Medicine. 2001 August 1; 164(3): 469-73.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11500352&dopt=Abstract

- **An unusual case of surgical emphysema in the neck following sport injury.**
  Author(s): Vattakuzhiyil GJ, Konstantinidis I.
  Source: The Journal of Laryngology and Otology. 2002 January; 116(1): 73-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11860663&dopt=Abstract

- **Anatomic landmarks to estimate the length of the diaphragm from chest radiographs: effects of emphysema and lung volume reduction surgery.**
  Author(s): Bellemare F, Couture J, Cordeau MP, Leblanc P, Lafontaine E.
  Source: Chest. 2001 August; 120(2): 444-52.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11502642&dopt=Abstract

- **Animal models of emphysema and their relevance to studies of particle-induced disease.**
  Author(s): March TH, Green FH, Hahn FF, Nikula KJ.
  Source: Inhalation Toxicology. 2000; 12 Suppl 4: 155-87. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12881891&dopt=Abstract

- **Animal models of emphysema: the next generations.**
  Author(s): Campbell EJ.
  Source: The Journal of Clinical Investigation. 2000 December; 106(12): 1445-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11120751&dopt=Abstract

- **Aortic root dilatation in patients with emphysema.**
  Author(s): Brasch AV, Mohsenifar Z, Jeon DS, Luo H, Mirocha JM, Khan SS, Siegel RJ.
  Source: American Heart Journal. 2001 December; 142(6): 1024-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11717607&dopt=Abstract

- **Apoptosis and emphysema: the missing link.**
  Author(s): Tuder RM, Petrache I, Elias JA, Voelkel NF, Henson PM.
  Source: American Journal of Respiratory Cell and Molecular Biology. 2003 May; 28(5): 551-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12707010&dopt=Abstract

- **Assessment of lung volumes in pulmonary emphysema using multidetector helical CT: comparison with pulmonary function tests.**
  Author(s): Arakawa A, Yamashita Y, Nakayama Y, Kadota M, Korogi H, Kawano O, Matsumoto M, Takahashi M.
  Source: Computerized Medical Imaging and Graphics : the Official Journal of the Computerized Medical Imaging Society. 2001 September-October; 25(5): 399-404.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11390194&dopt=Abstract

- **Association of CYP2A6 deletion polymorphism with smoking habit and development of pulmonary emphysema.**
  Author(s): Minematsu N, Nakamura H, Iwata M, Tateno H, Nakajima T, Takahashi S, Fujishima S, Yamaguchi K.
  Source: Thorax. 2003 July; 58(7): 623-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12832682&dopt=Abstract

- **Association of emphysema, gout, and inflammatory markers with long-term incidence of age-related maculopathy.**
  Author(s): Klein R, Klein BE, Tomany SC, Cruickshanks KJ.
  Source: Archives of Ophthalmology. 2003 May; 121(5): 674-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12742845&dopt=Abstract

- **Bilateral emphysematous pyelonephritis combined with subcapsular hematoma and disseminated necrotizing fasciitis.**
  Author(s): Lin DC, Shieh GS, Tong YC.
  Source: Urologia Internationalis. 2003; 70(3): 244-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12660468&dopt=Abstract

- **Bilateral emphysematous pyelonephritis with autosomal-dominant polycystic kidney disease successfully treated by conservative method.**
  Author(s): Shimizu H, Hariu K, Kamiyama Y, Tomomasa H, Iizumi T, Yazaki T, Umeda T.
  Source: Urologia Internationalis. 1999; 63(4): 252-4. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10743706&dopt=Abstract

- **Bilateral emphysematous pyelonephritis with perirenal abscess cured by conservative therapy.**
  Author(s): Lim CS, Kim WB, Kim YS, Ahn C, Han JS, Kim S, Lee JS.
  Source: Journal of Nephrology. 2000 March =april; 13(2): 155-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10858980&dopt=Abstract

- **Bilateral pneumothoraces, pneumomediastinum, pneumoperitoneum, pneumoretroperitoneum, and subcutaneous emphysema following intubation with a double-lumen endotracheal tube for thoracoscopic anterior spinal release and fusion in a patient with idiopathic scoliosis.**
  Author(s): Sucato DJ, Girgis M.
  Source: Journal of Spinal Disorders & Techniques. 2002 April; 15(2): 133-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11927822&dopt=Abstract

- **Bilateral pneumothorax with extensive subcutaneous emphysema manifested during third molar surgery. A case report.**
  Author(s): Sekine J, Irie A, Dotsu H, Inokuchi T.
  Source: International Journal of Oral and Maxillofacial Surgery. 2000 October; 29(5): 355-7. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11071238&dopt=Abstract

- **Bilateral subcutaneous emphysema of the orbits following nose blowing.**
  Author(s): Mohan B, Singh KP.
  Source: The Journal of Laryngology and Otology. 2001 April; 115(4): 319-20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11276340&dopt=Abstract

- **Body weight and nutritional changes after reduction pneumoplasty for severe emphysema: a randomized study.**
  Author(s): Mineo TC, Ambrogi V, Pompeo E, Bollero P, Mineo D, Nofroni I; Pulmonary Emphysema Research Group.
  Source: The Journal of Thoracic and Cardiovascular Surgery. 2002 October; 124(4): 660-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12324722&dopt=Abstract

- **Breathing out into water during subtotal immersion: a therapy for chronic pulmonary emphysema.**
  Author(s): Kurabayashi H, Machida I, Tamura K, Iwai F, Tamura J, Kubota K.
  Source: American Journal of Physical Medicine & Rehabilitation / Association of Academic Physiatrists. 2000 March-April; 79(2): 150-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10744189&dopt=Abstract

- **Bronchial atresia with mucocele in an adolescent girl: an uncommon cause of lobar emphysema.**
  Author(s): Wong KS, Wang CR, Lien R.
  Source: Monaldi Arch Chest Dis. 2000 October; 55(5): 375-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11213373&dopt=Abstract

- **Bronchial carcinoid tumor presenting with complete lobar collapse and unilateral lung emphysema.**
  Author(s): Liu S, Ko S, Chen W.
  Source: Clinical Imaging. 2000 May-June; 24(3): 159-61.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11150684&dopt=Abstract

- **Bronchial fenestration improves expiratory flow in emphysematous human lungs.**
  Author(s): Lausberg HF, Chino K, Patterson GA, Meyers BF, Toeniskoetter PD, Cooper JD.
  Source: The Annals of Thoracic Surgery. 2003 February; 75(2): 393-7; Discussion 398.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12607646&dopt=Abstract

- **Bronchiolitis obliterans syndrome in single lung transplant recipients--patients with emphysema versus patients with idiopathic pulmonary fibrosis.**
  Author(s): Haider Y, Yonan N, Mogulkoc N, Carroll KB, Egan JJ.
  Source: The Journal of Heart and Lung Transplantation : the Official Publication of the International Society for Heart Transplantation. 2002 March; 21(3): 327-33.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11897520&dopt=Abstract

- **Bronchoscopic volume reduction with valve implants in patients with severe emphysema.**
  Author(s): Toma TP, Hopkinson NS, Hillier J, Hansell DM, Morgan C, Goldstraw PG, Polkey MI, Geddes DM.
  Source: Lancet. 2003 March 15; 361(9361): 931-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12648974&dopt=Abstract

- **Bullae, bronchiectasis and nutritional emphysema in severe anorexia nervosa.**
  Author(s): Cook VJ, Coxson HO, Mason AG, Bai TR.
  Source: Can Respir J. 2001 September-October; 8(5): 361-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11694916&dopt=Abstract

- **Bullectomy is beneficial in the pulmonary blood flow/driving pressure relationship in bullous emphysema patients.**
  Author(s): Onuki T, Murasugi M, Sone Y, Ikeda T, Oyama K, Nitta S.
  Source: Jpn J Thorac Cardiovasc Surg. 2001 May; 49(5): 301-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11431949&dopt=Abstract

- **Bullectomy is comparable to lung volume reduction in patients with end-stage emphysema.**
  Author(s): De Giacomo T, Rendina EA, Venuta F, Moretti M, Mercadante E, Mohsen I, Filice MJ, Coloni GF.
  Source: European Journal of Cardio-Thoracic Surgery : Official Journal of the European Association for Cardio-Thoracic Surgery. 2002 September; 22(3): 357-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12204723&dopt=Abstract

- **Bullous emphysema after Legionella pneumonia in a two-year-old child.**
  Author(s): Gervaix A, Beghetti M, Rimensberger P, Posfay-Barbe K, Barazzone C.
  Source: The Pediatric Infectious Disease Journal. 2000 January; 19(1): 86-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10643861&dopt=Abstract

- **Can aerosol-derived airway morphometry detect early, asymptomatical lung emphysema?**
  Author(s): Brand P, Letzel S, Buchta M, Scheuch G, Windorfer K, Hilla W, Smith HJ, Kraus T.
  Source: Journal of Aerosol Medicine : the Official Journal of the International Society for Aerosols in Medicine. 2003 Summer; 16(2): 143-51.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12823908&dopt=Abstract

- **Can computed tomography predict functional benefit from lung volume reduction surgery for emphysema?**
  Author(s): Gevenois PA, Estenne M.
  Source: American Journal of Respiratory and Critical Care Medicine. 2001 December 15; 164(12): 2137-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11751173&dopt=Abstract

- **Cardiac morphology in lung volume reduction surgery for endstage emphysema.**
  Author(s): Vigneswaran WT, Chomka EV, Jelnin V, Hernan MJ, Podbielski FJ.
  Source: Asian Cardiovascular & Thoracic Annals. 2003 March; 11(1): 48-51.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12692023&dopt=Abstract

- **Cervical emphysema and pneumomediastinum after tonsillectomy: it can happen.**
  Author(s): Marioni G, De Filippis C, Tregnaghi A, Gaio E, Staffieri A.
  Source: Otolaryngology and Head and Neck Surgery. 2003 February; 128(2): 298-300.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12601334&dopt=Abstract

- **Cervical emphysema complicating tonsillectomy with argon beam coagulation.**
  Author(s): Fechner FP, Kieff D.
  Source: The Laryngoscope. 2003 May; 113(5): 920-1.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12792334&dopt=Abstract

- **Cervical subcutaneous emphysema after lower abdominal laparoscopic surgery.**
  Author(s): Jen A, Sanelli PC, Honrado C, Huang C.
  Source: Otolaryngology and Head and Neck Surgery. 2003 January; 128(1): 157-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12574778&dopt=Abstract

- **Cervical surgical emphysema: a rare presentation of a sigmoid colon retroperitoneal diverticular perforation.**
  Author(s): Basu S, Corless D.
  Source: Int J Clin Pract. 2002 April; 56(3): 222.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12018831&dopt=Abstract

- **Cervicofacial subcutaneous emphysema after lower root canal therapy.**
  Author(s): Penna KJ, Neshat K.
  Source: The New York State Dental Journal. 2001 May; 67(5): 28-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11452748&dopt=Abstract

- **Chronic bronchitis and emphysema: clearing the air.**
  Author(s): Wisniewski A.
  Source: Nursing. 2003 May; 33(5): 46-9. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12792571&dopt=Abstract

- **Chronic obstructive pulmonary disease - part 2: pathology and biochemistry of emphysema.**
  Author(s): Hogg JC, Senior RM.
  Source: Thorax. 2002 September; 57(9): 830-4. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12200530&dopt=Abstract

- **Cigarette smoke inhibits the growth of lung fibroblasts from patients with pulmonary emphysema.**
  Author(s): Nobukuni S, Watanabe K, Inoue J, Wen FQ, Tamaru N, Yoshida M.
  Source: Respirology (Carlton, Vic.). 2002 September; 7(3): 217-23.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12153687&dopt=Abstract

- **Classification of emphysema in candidates for lung volume reduction surgery: a new objective and surgically oriented model for describing CT severity and heterogeneity.**
  Author(s): Cederlund K, Tylen U, Jorfeldt L, Aspelin P.
  Source: Chest. 2002 August; 122(2): 590-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12171837&dopt=Abstract

- **Clinical characteristics of emphysematous pyelonephritis.**
  Author(s): Tang HJ, Li CM, Yen MY, Chen YS, Wann SR, Lin HH, Lee SS, Liu YC.
  Source: J Microbiol Immunol Infect. 2001 June; 34(2): 125-30.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11456358&dopt=Abstract

- **Cloning of dexamethasone-induced transcript: a novel glucocorticoid-induced gene that is upregulated in emphysema.**
  Author(s): Edgar AJ, Birks EJ, Yacoub MH, Polak JM.
  Source: American Journal of Respiratory Cell and Molecular Biology. 2001 July; 25(1): 119-24.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11472984&dopt=Abstract

- **Comparative study of mediastinal emphysema as determined by etiology.**
  Author(s): Kobashi Y, Okimoto N, Matsushima T, Soejima R.
  Source: Intern Med. 2002 April; 41(4): 277-82.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11993787&dopt=Abstract

- **Comparison of changes in hemodynamics between unilateral and bilateral lung volume reduction for pulmonary emphysema.**
  Author(s): Koizumi K, Haraguchi S, Akiyama H, Hirata T, Hirai K, Mikami I, Tanaka S.
  Source: Ann Thorac Cardiovasc Surg. 2001 October; 7(5): 266-72.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11743852&dopt=Abstract

- **Congenital lobar emphysema.**
  Author(s): Al-Salem AH.
  Source: Saudi Med J. 2002 March; 23(3): 335-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11938429&dopt=Abstract

- **Congenital lobar emphysema: a clinicopathologic evaluation of 14 cases.**
  Author(s): Tander B, Yalcin M, Yilmaz B, Ali Karadag C, Bulut M.
  Source: European Journal of Pediatric Surgery : Official Journal of Austrian Association of Pediatric Surgery. [et Al] = Zeitschrift Fur Kinderchirurgie. 2003 April; 13(2): 108-11.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12776242&dopt=Abstract

- **Congenital lobar emphysema: evaluation and long-term follow-up of thirty cases at a single center.**
  Author(s): Ozcelik U, Gocmen A, Kiper N, Dogru D, Dilber E, Yalcin EG.
  Source: Pediatric Pulmonology. 2003 May; 35(5): 384-91.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12687596&dopt=Abstract

- **Congenital lobar emphysema: Like father, like son.**
  Author(s): Roberts PA, Holland AJ, Halliday RJ, Arbuckle SM, Cass DT.
  Source: Journal of Pediatric Surgery. 2002 May; 37(5): 799-801.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11987106&dopt=Abstract

- **Continuous caudal epidural analgesia for congenital lobar emphysema: a report of three cases.**
  Author(s): Raghavendran S, Diwan R, Shah T, Vas L.
  Source: Anesthesia and Analgesia. 2001 August; 93(2): 348-50 , 3Rd Contents Page.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11473858&dopt=Abstract

- **Core to rind distribution of severe emphysema predicts outcome of lung volume reduction surgery.**
  Author(s): Nakano Y, Coxson HO, Bosan S, Rogers RM, Sciurba FC, Keenan RJ, Walley KR, Pare PD, Hogg JC.
  Source: American Journal of Respiratory and Critical Care Medicine. 2001 December 15; 164(12): 2195-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11751187&dopt=Abstract

- **Correlation among the indices of high-resolution computed tomography, pulmonary function tests, pulmonary perfusion scans and exercise tolerance in cases of chronic pulmonary emphysema.**
  Author(s): Fujita E, Nagasaka Y, Kozuka T, Ebara H, Fukuoka M.
  Source: Respiration; International Review of Thoracic Diseases. 2002; 69(1): 30-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11844960&dopt=Abstract

- **Cost effectiveness of lung-volume-reduction surgery for patients with severe emphysema.**
  Author(s): Ramsey SD, Berry K, Etzioni R, Kaplan RM, Sullivan SD, Wood DE; National Emphysema Treatment Trial Research Group.
  Source: The New England Journal of Medicine. 2003 May 22; 348(21): 2092-102. Epub 2003 May 20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12759480&dopt=Abstract

- **CT assessment of subtypes of pulmonary emphysema in smokers.**
  Author(s): Satoh K, Kobayashi T, Misao T, Hitani Y, Yamamoto Y, Nishiyama Y, Ohkawa M.
  Source: Chest. 2001 September; 120(3): 725-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11555499&dopt=Abstract

- **CT findings and temporal course of persistent pulmonary interstitial emphysema in neonates: a multiinstitutional study.**
  Author(s): Donnelly LF, Lucaya J, Ozelame V, Frush DP, Strouse PJ, Sumner TE, Paltiel HJ.
  Source: Ajr. American Journal of Roentgenology. 2003 April; 180(4): 1129-33.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12646469&dopt=Abstract

- **CT imaging of pulmonary lobar interstitial emphysema in a spontaneous breathing preterm infant.**
  Author(s): Dembinski J, Heep A, Kau N, Knopfle G, Bartmann P.
  Source: American Journal of Perinatology. 2002 August; 19(6): 285-90. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12357418&dopt=Abstract

- **CT of emphysema.**
  Author(s): Newell JD Jr.
  Source: Radiologic Clinics of North America. 2002 January; 40(1): 31-42, Vii. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11813818&dopt=Abstract

- **CT quantification of pulmonary emphysema: assessment of lung structure and function.**
  Author(s): Bankier AA, Madani A, Gevenois PA.
  Source: Crit Rev Comput Tomogr. 2002; 43(6): 399-417. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12521149&dopt=Abstract

- **Cutaneous emphysema and craniocervical bone pneumatization.**
  Author(s): Turowski B, Rettig J, Raab P, Zanella FE.
  Source: Ajnr. American Journal of Neuroradiology. 2001 August; 22(7): 1398-400.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11498436&dopt=Abstract

- **Delayed presentation of pulmonary interstitial emphysema.**
  Author(s): Cabana MD, Benson JE, Smith AE, Baggett HC, Northington FJ.
  Source: Clinical Pediatrics. 2000 May; 39(5): 299-302.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10826078&dopt=Abstract

- **Detection of emphysema in rat lungs by using magnetic resonance measurements of 3He diffusion.**
  Author(s): Chen XJ, Hedlund LW, Moller HE, Chawla MS, Maronpot RR, Johnson GA.
  Source: Proceedings of the National Academy of Sciences of the United States of America. 2000 October 10; 97(21): 11478-81.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11027348&dopt=Abstract

- **Diagnostic dilemma. Emphysematous cystitis.**
  Author(s): Tsao JW, Jun SL.
  Source: The American Journal of Medicine. 2001 February 15; 110(3): 220, 239.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11221634&dopt=Abstract

- **Differential gene expression of sFRP-1 and apoptosis in pulmonary emphysema.**
  Author(s): Imai K, D'Armiento J.
  Source: Chest. 2002 March; 121(3 Suppl): 7S.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11893652&dopt=Abstract

- **Differential lung ventilation after single-lung transplantation for emphysema.**
  Author(s): Mitchell JB, Shaw AD, Donald S, Farrimond JG.
  Source: Journal of Cardiothoracic and Vascular Anesthesia. 2002 August; 16(4): 459-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12154426&dopt=Abstract

- **Direct medical costs of chronic obstructive pulmonary disease: chronic bronchitis and emphysema.**
  Author(s): Wilson L, Devine EB, So K.
  Source: Respiratory Medicine. 2000 March; 94(3): 204-13.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10783930&dopt=Abstract

- **Disruption of the klotho gene causes pulmonary emphysema in mice. Defect in maintenance of pulmonary integrity during postnatal life.**
  Author(s): Suga T, Kurabayashi M, Sando Y, Ohyama Y, Maeno T, Maeno Y, Aizawa H, Matsumura Y, Kuwaki T, Kuro-O M, Nabeshima Y, Nagai R.
  Source: American Journal of Respiratory Cell and Molecular Biology. 2000 January; 22(1): 26-33.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10615062&dopt=Abstract

- **Distribution of lung density and mass in patients with emphysema as assessed by quantitative analysis of CT.**
  Author(s): Diallo MH, Guenard H, Laurent F, Carles P, Giron J.
  Source: Chest. 2000 December; 118(6): 1566-75.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11115441&dopt=Abstract

- **Distribution of ventilation-to-perfusion ratios analysed in planar scintigrams of emphysematous patients.**
  Author(s): Xu JH, Moonen M, Johansson A, Bake B.
  Source: Clinical Physiology (Oxford, England). 2000 March; 20(2): 89-94.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10735974&dopt=Abstract

- **Double cancers of the kidney and ureter complicated with emphysematous pyelonephritis within the parenchyma of the renal tumour.**
  Author(s): Wang MC, Tseng CC, Lan RR, Lin CY, Chen FF, Huang JJ.
  Source: Scandinavian Journal of Urology and Nephrology. 1999 December; 33(6): 420-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10636588&dopt=Abstract

- **Dynamic echo planar MR imaging of lung ventilation with hyperpolarized (3)He in normal subjects and patients with severe emphysema.**
  Author(s): Gierada DS, Saam B, Yablonskiy D, Cooper JD, Lefrak SS, Conradi MS.
  Source: Nmr in Biomedicine. 2000 June; 13(4): 176-81.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10867693&dopt=Abstract

- **ED ultrasound: emphysematous pyelitis.**
  Author(s): Chong CF, Wang TL, Chang H.
  Source: The American Journal of Emergency Medicine. 2002 July; 20(4): 368-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12098188&dopt=Abstract

- **Effect of lung volume reduction surgery for severe emphysema on right ventricular function.**
  Author(s): Mineo TC, Pompeo E, Rogliani P, Dauri M, Turani F, Bollero P, Magliocchetti N.
  Source: American Journal of Respiratory and Critical Care Medicine. 2002 February 15; 165(4): 489-94.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11850341&dopt=Abstract

- **Effects of emphysema and lung volume reduction surgery on transdiaphragmatic pressure and diaphragm length.**
  Author(s): Bellemare F, Cordeau MP, Couture J, Lafontaine E, Leblanc P, Passerini L.
  Source: Chest. 2002 June; 121(6): 1898-910.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12065355&dopt=Abstract

- **Effects of lung volume reduction surgery for emphysema on oxygen cost of breathing.**
  Author(s): Takayama T, Shindoh C, Kurokawa Y, Hida W, Kurosawa H, Ogawa H, Satomi S.
  Source: Chest. 2003 June; 123(6): 1847-52.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12796159&dopt=Abstract

- **Efficacy of microdrainage in severe subcutaneous emphysema.**
  Author(s): Leo F, Solli P, Veronesi G, Spaggiari L, Pastorino U.
  Source: Chest. 2002 October; 122(4): 1498-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12377895&dopt=Abstract

- **Emphysema due to alpha-antitrypsin deficiency: familial study of the YBARCELONA variant.**
  Author(s): Miravitlles M, Vila S, Jardi R, de la Roza C, Rodriguez-Frias F, Vidal R.
  Source: Chest. 2003 July; 124(1): 404-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12853554&dopt=Abstract

- **Emphysema in heavy smokers with normal chest radiography. Detection and quantification by HCRT.**
  Author(s): Sashidhar K, Gulati M, Gupta D, Monga S, Suri S.
  Source: Acta Radiologica (Stockholm, Sweden : 1987). 2002 January; 43(1): 60-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11972464&dopt=Abstract

- **Emphysema in nonsmokers: alpha 1-antitrypsin deficiency and other causes.**
  Author(s): Lee P, Gildea TR, Stoller JK.
  Source: Cleve Clin J Med. 2002 December; 69(12): 928-9, 933, 936 Passim. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12546267&dopt=Abstract

- **Emphysema of the knee and thigh following excessive use of the Mitek vaporizer during arthroscopy of the knee.**
  Author(s): Logan AJ, Roy S, Wilson C.
  Source: Clinical Journal of Sport Medicine : Official Journal of the Canadian Academy of Sport Medicine. 2002 May; 12(3): 182-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12011727&dopt=Abstract

- **Emphysematous changes are caused by degradation of type III collagen in transgenic mice expressing MMP-1.**
  Author(s): Shiomi T, Okada Y, Foronjy R, Schiltz J, Jaenish R, Krane S, D'Armiento J.
  Source: Experimental Lung Research. 2003 January-February; 29(1): 1-15.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12652812&dopt=Abstract

- **Emphysematous cholecystitis.**
  Author(s): Lallemand B, De Keuleneer R, Maassarani F.
  Source: Acta Chir Belg. 2003 April; 103(2): 230-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12768870&dopt=Abstract

- **Emphysematous cholecystitis: sonographic findings.**
  Author(s): Konno K, Ishida H, Naganuma H, Sato M, Komatsuda T, Sato A, Ishida J, Sakai T, Watanabe S.
  Source: Abdominal Imaging. 2002 March-April; 27(2): 191-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11847580&dopt=Abstract

- **Emphysematous cystitis, a rare complication of urinary tract infection in a male diabetic patient: a case report.**
  Author(s): Hsin SC, Hsieh MC, Lin HY, Hsia PJ, Shin SJ.
  Source: Kaohsiung J Med Sci. 2003 March; 19(3): 132-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12751874&dopt=Abstract

- **Emphysematous cystitis: a case report.**
  Author(s): Bartczak J, Schiedermayer D.
  Source: Wmj. 1999 December; 98(8): 49-50. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10639896&dopt=Abstract

- **Emphysematous gastritis and severe aplastic anemia.**
  Author(s): Gutierrez O, Cantalapiedra A, Tabuyo MI, Del Villar R, Penarrubia MJ, Sales R, Garcia-Frade LJ.
  Source: The Hematology Journal : the Official Journal of the European Haematology Association / Eha. 2003; 4(1): 82-4. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12692527&dopt=Abstract

- **Emphysematous gastritis associated with gastric infarction in a patient with adult polycystic renal disease: CT diagnosis.**
  Author(s): Wong YY, Chu WC.
  Source: Ajr. American Journal of Roentgenology. 2002 May; 178(5): 1291.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11959754&dopt=Abstract

- **Emphysematous gastritis in a hemodialysis patient.**
  Author(s): Yalamanchili M, Cady W.
  Source: Southern Medical Journal. 2003 January; 96(1): 84-8. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12602725&dopt=Abstract

- **Emphysematous infections of the abdomen and pelvis: a pictorial review.**
  Author(s): Grayson DE, Abbott RM, Levy AD, Sherman PM.
  Source: Radiographics : a Review Publication of the Radiological Society of North America, Inc. 2002 May-June; 22(3): 543-61. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12006686&dopt=Abstract

- **Emphysematous pancreatitis.**
  Author(s): Birgisson H, Stefansson T, Andresdottir A, Moller PH.
  Source: The European Journal of Surgery = Acta Chirurgica. 2001 December; 167(12): 918-20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11841083&dopt=Abstract

- **Emphysematous pyelitis presenting as an acute abdomen in an end-stage renal disease patient treated with peritoneal dialysis.**
  Author(s): Anwar N, Chawla LS, Lew SQ.
  Source: American Journal of Kidney Diseases : the Official Journal of the National Kidney Foundation. 2002 October; 40(4): E13.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12324934&dopt=Abstract

- **Emphysematous pyelonephritis recovered by ureteral stenting in a functionally solitary kidney.**
  Author(s): Ku JH, Kim ME, Lee NK, Park YH.
  Source: Urologia Internationalis. 2002; 69(4): 321-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12444293&dopt=Abstract

- **Emphysematous pyelonephritis.**
  Author(s): Goichot B, Andres E.
  Source: The New England Journal of Medicine. 2000 January 6; 342(1): 60-1.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10627217&dopt=Abstract

- **Emphysematous pyelonephritis.**
  Author(s): Sean TG, Sheshadri S, Saravu K.
  Source: J Assoc Physicians India. 2002 November; 50: 1413-5. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12583474&dopt=Abstract

- **Endotracheal intubation related massive subcutaneous emphysema and tension pneumomediastinum resulting in cardiac arrest.**
  Author(s): Pandey M, Jain A, Mehta A, Sharma M.
  Source: Journal of Postgraduate Medicine. 2003 April-June; 49(2): 188-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12867707&dopt=Abstract

- **Epidemiology of emphysema in subjects with severe alpha 1-antitrypsin deficiency.**
  Author(s): Seersholm N.
  Source: Dan Med Bull. 2002 May; 49(2): 145-58. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12064091&dopt=Abstract

- **Epidural emphysema associated with primary spontaneous pneumothorax.**
  Author(s): Aribas OK, Gormus N, Aydogdu Kiresi D.
  Source: European Journal of Cardio-Thoracic Surgery : Official Journal of the European Association for Cardio-Thoracic Surgery. 2001 September; 20(3): 645-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11509299&dopt=Abstract

- **Evaluation of bronchodilator responses in patients with "irreversible" emphysema.**
  Author(s): Kummer F.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2002 May; 19(5): 981-2; Author Reply 982-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12030743&dopt=Abstract

- **Evaluation of emphysema in patients with asthma using high-resolution CT.**
  Author(s): Hong KY, Lee JH, Park SW, Joo JH, Kim do J, Moon SH, Uh ST, Kim YH, Park CS, Park JS.
  Source: Korean J Intern Med. 2002 March; 17(1): 24-30.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12014209&dopt=Abstract

- **Extensive craniofacial subcutaneous emphysema after evacuation of a chronic subdural haematoma.**
  Author(s): Joanes V, Gallego JM.
  Source: Acta Neurochirurgica. 2003 August; 145(8): 713-4; Discussion 714.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14520554&dopt=Abstract

- **Extensive subcutaneous emphysema following arthroscopy: a case report.**
  Author(s): Deshmukh NV, Shah MM.
  Source: Knee Surgery, Sports Traumatology, Arthroscopy : Official Journal of the Esska. 2002 March; 10(2): 119-21. Epub 2002 January 30.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11914770&dopt=Abstract

- **Fallingwater and emphysema.**
  Author(s): Fessler HE.
  Source: American Journal of Respiratory and Critical Care Medicine. 2001 November 15; 164(10 Pt 1): 1753-4. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11734415&dopt=Abstract

- **Familial related risk-factors in the development of chronic bronchitis/emphysema as compared to asthma assessed in a postal survey.**
  Author(s): Montnemery P, Lanke J, Lindholm LH, Lundback B, Nyberg P, Adelroth E, Lofdahl CG.
  Source: European Journal of Epidemiology. 2000; 16(11): 1003-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11421467&dopt=Abstract

- **Fatal emphysematous pyelonephritis with gas in the spinal extradural space in a patient with diabetes.**
  Author(s): Sailesh S, Randeva HS, Hillhouse EW, Patel V.
  Source: Diabetic Medicine : a Journal of the British Diabetic Association. 2001 January; 18(1): 68-71.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11168344&dopt=Abstract

- **Feasibility and safety of the airway bypass procedure for patients with emphysema.**
  Author(s): Rendina EA, De Giacomo T, Venuta F, Coloni GF, Meyers BF, Patterson GA, Cooper JD.
  Source: The Journal of Thoracic and Cardiovascular Surgery. 2003 June; 125(6): 1294-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12830047&dopt=Abstract

- **Fractal analysis of nuclear medicine images for the diagnosis of pulmonary emphysema: interpretations, implications, and limitations.**
  Author(s): Chung HW, Huang YH.
  Source: Ajr. American Journal of Roentgenology. 2000 April; 174(4): 1055-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10749249&dopt=Abstract

- **Gain and subsequent loss of lung function after lung volume reduction surgery in cases of severe emphysema with different morphologic patterns.**
  Author(s): Bloch KE, Georgescu CL, Russi EW, Weder W.
  Source: The Journal of Thoracic and Cardiovascular Surgery. 2002 May; 123(5): 845-54.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12019368&dopt=Abstract

- **Gas within the wall of the stomach due to emphysematous gastritis: case report and review.**
  Author(s): van Mook WN, van der Geest S, Goessens ML, Schoon EJ, Ramsay G.
  Source: European Journal of Gastroenterology & Hepatology. 2002 October; 14(10): 1155-60. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12362108&dopt=Abstract

- **Gene polymorphism for microsomal epoxide hydrolase and susceptibility to emphysema in a Japanese population.**
  Author(s): Takeyabu K, Yamaguchi E, Suzuki I, Nishimura M, Hizawa N, Kamakami Y.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2000 May; 15(5): 891-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10853854&dopt=Abstract

- **Genetic polymorphism in matrix metalloproteinase-9 and pulmonary emphysema.**
  Author(s): Minematsu N, Nakamura H, Tateno H, Nakajima T, Yamaguchi K.
  Source: Biochemical and Biophysical Research Communications. 2001 November 23; 289(1): 116-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11708786&dopt=Abstract

- **Giant bullous emphysema resection by VATS. Analysis of laser and stapler techniques.**
  Author(s): Divisi D, Battaglia C, Di Francescantonio W, Torresini G, Crisci R.
  Source: European Journal of Cardio-Thoracic Surgery : Official Journal of the European Association for Cardio-Thoracic Surgery. 2002 December; 22(6): 990-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12467825&dopt=Abstract

- **Guidance concerning surgery for emphysema.**
  Author(s): Drazen JM, Epstein AM.
  Source: The New England Journal of Medicine. 2003 May 22; 348(21): 2134-6. Epub 2003 May 20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12759481&dopt=Abstract

- **Hemodynamic characterization of patients with severe emphysema.**
  Author(s): Scharf SM, Iqbal M, Keller C, Criner G, Lee S, Fessler HE; National Emphysema Treatment Trial (NETT) Group.
  Source: American Journal of Respiratory and Critical Care Medicine. 2002 August 1; 166(3): 314-22.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12153963&dopt=Abstract

- **Hereditary pulmonary emphysema.**
  Author(s): Bense L, Eklund G, Lewander R.
  Source: Chest. 2002 January; 121(1): 297-300.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11796471&dopt=Abstract

- **HOX genes in human lung: altered expression in primary pulmonary hypertension and emphysema.**
  Author(s): Golpon HA, Geraci MW, Moore MD, Miller HL, Miller GJ, Tuder RM, Voelkel NF.
  Source: American Journal of Pathology. 2001 March; 158(3): 955-66.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11238043&dopt=Abstract

- **Human collagenase (matrix metalloproteinase-1) expression in the lungs of patients with emphysema.**
  Author(s): Imai K, Dalal SS, Chen ES, Downey R, Schulman LL, Ginsburg M, D'Armiento J.
  Source: American Journal of Respiratory and Critical Care Medicine. 2001 March; 163(3 Pt 1): 786-91.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11254539&dopt=Abstract

- **Hypothalamic digoxin, hemispheric chemical dominance, and chronic bronchitis emphysema.**
  Author(s): Kurup RK, Kurup PA.
  Source: The International Journal of Neuroscience. 2003 September; 113(9): 1241-58.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12959742&dopt=Abstract

- **Images in clinical medicine. Centrilobular emphysema with predominantly upper-lobe involvement.**
  Author(s): Hunsaker AR, Reilly JJ.
  Source: The New England Journal of Medicine. 2003 May 22; 348(21): 2091.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12761366&dopt=Abstract

- **Images in clinical medicine. Emphysematous cholecystitis.**
  Author(s): Sakai Y.
  Source: The New England Journal of Medicine. 2003 June 5; 348(23): 2329.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12788997&dopt=Abstract

- **Images in clinical medicine. Emphysematous cystitis.**
  Author(s): Asada S, Kawasaki T.
  Source: The New England Journal of Medicine. 2003 July 17; 349(3): 258.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12867609&dopt=Abstract

- **Images in clinical medicine. Pneumomediastinum and severe subcutaneous emphysema.**
  Author(s): van der Kleij FG, Zijlstra JG.
  Source: The New England Journal of Medicine. 2000 May 4; 342(18): 1333.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10793166&dopt=Abstract

- **Images in clinical radiology. Extensive emphysematous cholecystitis.**
  Author(s): Coulier B, Cloots V.
  Source: Jbr-Btr. 1999 October; 82(5): 245. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10589177&dopt=Abstract

- **Improved long-term survival seen after lung volume reduction surgery compared to continued medical therapy for emphysema.**
  Author(s): Meyers BF, Yusen RD, Lefrak SS, Cooper JD.
  Source: The Annals of Thoracic Surgery. 2001 June; 71(6): 2081.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11426814&dopt=Abstract

- **Improved ventilatory function after combined operation for pulmonary emphysema and lung cancer.**
  Author(s): Sinjan EA, Van Schil PE, Ortmanns P, Van den Brande F, Hendriks JM, Eyskens E.
  Source: Int Surg. 1999 July-September; 84(3): 185-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10533773&dopt=Abstract

- **Increased effective lung volume following lung volume reduction surgery in emphysema.**
  Author(s): Homan S, Porter S, Peacock M, Saccoia N, Southcott AM, Ruffin R.
  Source: Chest. 2001 October; 120(4): 1157-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11591554&dopt=Abstract

- **Increased FDG uptake in the right cardiac chambers in a patient with pulmonary emphysema.**
  Author(s): Duarte PS, Zhuang H, Machado C, Aldighieri F, Martins LR, Alonso G.
  Source: Clinical Nuclear Medicine. 2002 August; 27(8): 605-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12170014&dopt=Abstract

- **Increased levels of interleukin-8 in BAL fluid from smokers susceptible to pulmonary emphysema.**
  Author(s): Tanino M, Betsuyaku T, Takeyabu K, Tanino Y, Yamaguchi E, Miyamoto K, Nishimura M.
  Source: Thorax. 2002 May; 57(5): 405-11.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11978916&dopt=Abstract

- **Increased susceptibility to pulmonary emphysema among HIV-seropositive smokers.**
  Author(s): Diaz PT, King MA, Pacht ER, Wewers MD, Gadek JE, Nagaraja HN, Drake J, Clanton TL.
  Source: Annals of Internal Medicine. 2000 March 7; 132(5): 369-72.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10691587&dopt=Abstract

- **Inducible targeting of IL-13 to the adult lung causes matrix metalloproteinase- and cathepsin-dependent emphysema.**
  Author(s): Zheng T, Zhu Z, Wang Z, Homer RJ, Ma B, Riese RJ Jr, Chapman HA Jr, Shapiro SD, Elias JA.
  Source: The Journal of Clinical Investigation. 2000 November; 106(9): 1081-93.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11067861&dopt=Abstract

- **Infantile lobar emphysema and tracheal bronchus in a patient with congenital heart disease.**
  Author(s): Elmaci TT, Guler N, Aydogan U, Onursal E.
  Source: Journal of Pediatric Surgery. 2001 October; 36(10): 1596-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11584419&dopt=Abstract

- **Infectious emphysematous gastritis in multiple sclerosis.**
  Author(s): Buyl L, Smeets P, Verstraete K.
  Source: Jbr-Btr. 2003 May-June; 86(3): 148-9. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12880158&dopt=Abstract

- **Interactions of regional respiratory mechanics and pulmonary ventilatory impairment in pulmonary emphysema: assessment with dynamic MRI and xenon-133 single-photon emission CT.**
  Author(s): Suga K, Tsukuda T, Awaya H, Matsunaga N, Sugi K, Esato K.
  Source: Chest. 2000 June; 117(6): 1646-55.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10858397&dopt=Abstract

- **Interferon gamma induction of pulmonary emphysema in the adult murine lung.**
  Author(s): Wang Z, Zheng T, Zhu Z, Homer RJ, Riese RJ, Chapman HA Jr, Shapiro SD, Elias JA.
  Source: The Journal of Experimental Medicine. 2000 December 4; 192(11): 1587-600.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11104801&dopt=Abstract

- **Intrapartum subcutaneous emphysema and pneumomediastinum.**
  Author(s): Potdar N, Tumula S, Roberts L.
  Source: Journal of Obstetrics and Gynaecology : the Journal of the Institute of Obstetrics and Gynaecology. 2003 January; 23(1): 80.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12647709&dopt=Abstract

- **Laparoscopic management and clinical outcome of emphysematous cholecystitis.**
  Author(s): Hazey JW, Brody FJ, Rosenblatt SM, Brodsky J, Malm J, Ponsky JL.
  Source: Surgical Endoscopy. 2001 October; 15(10): 1217-20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11727104&dopt=Abstract

- **Large subconjunctival emphysema causing diplopia and lagophthalmos.**
  Author(s): Kaiserman I.
  Source: Eur J Ophthalmol. 2003 January-February; 13(1): 86-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12635680&dopt=Abstract

- **Life-threatening upper airway obstruction in a child caused by retropharyngeal emphysema.**
  Author(s): Skogvoll E, Grammeltvedt AT, Aadahl P, Mostad U, Slordahl S.
  Source: Acta Anaesthesiologica Scandinavica. 2001 March; 45(3): 393-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11207480&dopt=Abstract

- **Liquid ventilation in an infant with persistent interstitial pulmonary emphysema.**
  Author(s): Dani C, Reali MF, Bertini G, Martelli E, Rubaltelli FF.
  Source: Journal of Perinatal Medicine. 2001; 29(2): 158-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11344676&dopt=Abstract

- **Lobar emphysema due to ductus arteriosus compressing right upper bronchus in an infant with congenital heart disease.**
  Author(s): Hishitani T, Ogawa K, Hoshino K, Nakamura Y, Iwanaka T, Masago K, Suzuki M.
  Source: The Annals of Thoracic Surgery. 2003 April; 75(4): 1308-10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12683583&dopt=Abstract

- **Lobar pulmonary interstitial emphysema in a premature infant on continuous positive airway pressure using nasal prongs.**
  Author(s): Gessler P, Toenz M, Gugger M, Pfenninger J.
  Source: European Journal of Pediatrics. 2001 April; 160(4): 263-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11317654&dopt=Abstract

- **Lobar volume reduction surgery: a method of increasing the lung cancer resection rate in patients with emphysema.**
  Author(s): Edwards JG, Duthie DJ, Waller DA.
  Source: Thorax. 2001 October; 56(10): 791-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11562519&dopt=Abstract

- **Local interstitial emphysema caused by meconium aspiration: report of one case.**
  Author(s): Cheng CY, Soong WJ.
  Source: Acta Paediatr Taiwan. 2001 July-August; 42(4): 236-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11550413&dopt=Abstract

- **Long-term outcome of bilateral lung volume reduction in 250 consecutive patients with emphysema.**
  Author(s): Ciccone AM, Meyers BF, Guthrie TJ, Davis GE, Yusen RD, Lefrak SS, Patterson GA, Cooper JD.
  Source: The Journal of Thoracic and Cardiovascular Surgery. 2003 March; 125(3): 513-25.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12658193&dopt=Abstract

- **Loss of integrin alpha(v)beta6-mediated TGF-beta activation causes Mmp12-dependent emphysema.**
  Author(s): Morris DG, Huang X, Kaminski N, Wang Y, Shapiro SD, Dolganov G, Glick A, Sheppard D.
  Source: Nature. 2003 March 13; 422(6928): 169-73.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12634787&dopt=Abstract

- **Lung function 5 yr after lung volume reduction surgery for emphysema.**
  Author(s): Gelb AF, McKenna RJ Jr, Brenner M, Epstein JD, Zamel N.
  Source: American Journal of Respiratory and Critical Care Medicine. 2001 June; 163(7): 1562-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11401874&dopt=Abstract

- **Lung transplantation for emphysema: two lungs or one.**
  Author(s): Weill D, Keshavjee S.
  Source: The Journal of Heart and Lung Transplantation : the Official Publication of the International Society for Heart Transplantation. 2001 July; 20(7): 739-42. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11448800&dopt=Abstract

- **Lung transplantation versus lung volume reduction as surgical therapy for emphysema.**
  Author(s): Meyers BF, Patterson GA.
  Source: World Journal of Surgery. 2001 February; 25(2): 238-43. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11338027&dopt=Abstract

- **Lung volume reduction surgery (LVRS) for emphysema: initial experience at the University Hospital Gasthuisberg. Leuven LVRS Group.**
  Author(s): Verpeut AC, Verleden GM, Van Raemdonck D, Decramer M, Lerut T, Demedts M.
  Source: Acta Clin Belg. 2000 May-June; 55(3): 154-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10981323&dopt=Abstract

- **Lung volume reduction surgery and nutritional status in patients with severe emphysema.**
  Author(s): Nezu K, Kawaguchi T, Kimura M, Yasukawa M, Kushibe K, Taniguchi S, Yoshikawa M.
  Source: Jpn J Thorac Cardiovasc Surg. 2001 September; 49(9): 552-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11577445&dopt=Abstract

- **Lung volume reduction surgery for emphysema.**
  Author(s): Flaherty KR, Martinez FJ.
  Source: Clinics in Chest Medicine. 2000 December; 21(4): 819-48. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11194788&dopt=Abstract

- **Lung volume reduction surgery for emphysema: correlation of CT and V/Q imaging with physiologic mechanisms of improvement in lung function.**
  Author(s): Hunsaker AR, Ingenito EP, Reilly JJ, Costello P.
  Source: Radiology. 2002 February; 222(2): 491-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11818618&dopt=Abstract

- **Lung volume reduction surgery for the treatment of severe emphysema: a study in a single Canadian institution.**
  Author(s): Tan AL, Unruh HW, Mink SN.
  Source: Canadian Journal of Surgery. Journal Canadien De Chirurgie. 2000 October; 43(5): 369-76.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11045096&dopt=Abstract

- **Lung volume reduction surgery in a ventilated patient with severe pulmonary emphysema.**
  Author(s): Murtuza B, Keogh BF, Simonds AK, Pepper JR.
  Source: The Annals of Thoracic Surgery. 2001 March; 71(3): 1037-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11269428&dopt=Abstract

- **Lung volume reduction surgery in emphysema: a systematic review.**
  Author(s): Stirling GR, Babidge WJ, Peacock MJ, Smith JA, Matar KS, Snell GI, Colville DJ, Maddern GJ.
  Source: The Annals of Thoracic Surgery. 2001 August; 72(2): 641-8. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11515927&dopt=Abstract

- **Lung volume reduction surgery in lieu of pneumonectomy in an infant with severe unilateral pulmonary interstitial emphysema.**
  Author(s): Messineo A, Fusaro F, Mognato G, Sabatti M, D'Amore ES, Guglielmi M.
  Source: Pediatric Pulmonology. 2001 May; 31(5): 389-93.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11340686&dopt=Abstract

- **Lung volume reduction surgery versus conservative treatment in severe emphysema.**
  Author(s): Wilkens H, Demertzis S, Konig J, Leitnaker CK, Schafers HJ, Sybrecht GW.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2000 December; 16(6): 1043-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11292103&dopt=Abstract

- **Lung volume reduction surgery: new hope for emphysema patients.**
  Author(s): Schedel EM, Connolly MA.
  Source: Dimensions of Critical Care Nursing : Dccn. 1999 January-February; 18(1): 28-34. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10639997&dopt=Abstract

- **Lymphocyte population and apoptosis in the lungs of smokers and their relation to emphysema.**
  Author(s): Majo J, Ghezzo H, Cosio MG.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2001 May; 17(5): 946-53.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11488331&dopt=Abstract

- **Magnetic resonance analysis of abnormal diaphragmatic motion in patients with emphysema.**
  Author(s): Iwasawa T, Kagei S, Gotoh T, Yoshiike Y, Matsushita K, Kurihara H, Saito K, Matsubara S.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2002 February; 19(2): 225-31.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11866002&dopt=Abstract

- **Malfunction of a unipolar pacemaker system following development of marked subcutaneous emphysema.**
  Author(s): Schlegel M, Horler R, Maier-Wolfle M, Rickli H.
  Source: Schweiz Med Wochenschr. 2000 December 2; 130(48): 1845-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11132528&dopt=Abstract

- **Malignant bronchosubcutaneous fistula presenting as subcutaneous emphysema.**
  Author(s): Fraser A, Nolan RL.
  Source: Journal of Thoracic Imaging. 2002 October; 17(4): 319-21.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12362072&dopt=Abstract

- **Massive subcutaneous emphysema after blunt tracheal rupture.**
  Author(s): Endara SA, Bidstrup BP.
  Source: The Journal of Trauma. 2001 April; 50(4): 761.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11303183&dopt=Abstract

- **Massive subcutaneous emphysema and hypercarbia: complications of carbon dioxide absorption during extraperitoneal and intraperitoneal laparoscopic surgery--case studies.**
  Author(s): Worrell JB, Cleary DT.
  Source: Aana Journal. 2002 December; 70(6): 456-61.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12526151&dopt=Abstract

- **Massive subcutaneous emphysema following percutaneous tracheostomy.**
  Author(s): Kaylie DM, Wax MK.
  Source: American Journal of Otolaryngology. 2002 September-October; 23(5): 300-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12239698&dopt=Abstract

- **Mediastinal emphysema after a minor oral laceration.**
  Author(s): Abdulla SR, Sen A.
  Source: Emergency Medicine Journal : Emj. 2002 March; 19(2): 182.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11904279&dopt=Abstract

- **Mediastinalemphysema after laparoscopic gastric banding.**
  Author(s): Lanthaler M, Weiss H, Weissenboeck E, Freund M, Aigner F, Nehoda H.
  Source: Surgical Endoscopy. 2003 April; 17(4): 661. Epub 2003 January 28.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12545271&dopt=Abstract

- **Metastatic gas gangrene of the leg due to acute emphysematous cholecystitis.**
  Author(s): Ito T, Shiraki K, Sekoguchi K, Hamada M, Yamanaka T, Takase K, Nakano T.
  Source: Digestive Diseases and Sciences. 2001 November; 46(11): 2480-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11713957&dopt=Abstract

- **Microsatellite polymorphism in the heme oxygenase-1 gene promoter is associated with susceptibility to emphysema.**
  Author(s): Yamada N, Yamaya M, Okinaga S, Nakayama K, Sekizawa K, Shibahara S, Sasaki H.
  Source: American Journal of Human Genetics. 2000 January; 66(1): 187-95. Erratum In: Am J Hum Genet 2001 June; 68(6): 1542.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10631150&dopt=Abstract

- **Monocytic leukemia with CALM/AF10 rearrangement showing mediastinal emphysema.**
  Author(s): Nakamura F, Maki K, Arai Y, Nakamura Y, Mitani K.
  Source: American Journal of Hematology. 2003 February; 72(2): 138-42.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12555219&dopt=Abstract

- **Morbidity and mortality related to the native lung in single lung transplantation for emphysema.**
  Author(s): Mal H, Brugiere O, Sleiman C, Rullon I, Jebrak G, Groussard O, Reffas T, Stern JB, Leseche G, Fournier M.
  Source: The Journal of Heart and Lung Transplantation : the Official Publication of the International Society for Heart Transplantation. 2000 February; 19(2): 220-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10703700&dopt=Abstract

- **More inflammation than lung in emphysema.**
  Author(s): Calhoun WJ.
  Source: American Journal of Respiratory and Critical Care Medicine. 2002 March 1; 165(5): 730-1.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11874825&dopt=Abstract

- **Morphologic grading of emphysema is useful in the selection of candidates for unilateral or bilateral reduction pneumoplasty.**
  Author(s): Pompeo E, Sergiacomi G, Nofroni I, Roscetti W, Simonetti G, Mineo TC.
  Source: European Journal of Cardio-Thoracic Surgery : Official Journal of the European Association for Cardio-Thoracic Surgery. 2000 June; 17(6): 680-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10856859&dopt=Abstract

- **Morphological quantification of emphysema in small human lung specimens: comparison of methods and relation with clinical data.**
  Author(s): Robbesom AA, Versteeg EM, Veerkamp JH, van Krieken JH, Bulten HJ, Smits HT, Willems LN, van Herwaarden CL, Dekhuijzen PN, van Kuppevelt TH.
  Source: Modern Pathology : an Official Journal of the United States and Canadian Academy of Pathology, Inc. 2003 January; 16(1): 1-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12527706&dopt=Abstract

- **Morphometric investigation of emphysema aquosum in the elderly.**
  Author(s): Kohlhase C, Maxeiner H.
  Source: Forensic Science International. 2003 July 8; 134(2-3): 93-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12850401&dopt=Abstract

- **Near normalization of spirometry in a subject with severe emphysema complicated by amiodarone lung.**
  Author(s): Cockcroft DW, Fisher KL.
  Source: Respiratory Medicine. 1999 August; 93(8): 597-600.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10542995&dopt=Abstract

- **Neonatal air leaks: pneumothorax, pneumomediastinum, pulmonary interstitial emphysema, pneumopericardium.**
  Author(s): Carey B.
  Source: Neonatal Netw. 1999 December; 18(8): 81-4. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11885076&dopt=Abstract

- **Neutrophil-associated activation markers in healthy smokers relates to a fall in DL(CO) and to emphysematous changes on high resolution CT.**
  Author(s): Ekberg-Jansson A, Andersson B, Bake B, Boijsen M, Enanden I, Rosengren A, Skoogh BE, Tylen U, Venge P, Lofdahl CG.
  Source: Respiratory Medicine. 2001 May; 95(5): 363-73.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11392577&dopt=Abstract

- **New hope for patients with emphysema: lung volume reduction surgery.**
  Author(s): Baker S, Flynn MB.
  Source: Heart & Lung : the Journal of Critical Care. 1999 November-December; 28(6): 455-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10580219&dopt=Abstract

- **New National Emphysema Treatment Trial paradigm of Health Care Financing Administration-sponsored clinical research trials: advances and dilemmas.**
  Author(s): Brenner M, Jones B, Daneschvar HL, Triff S.
  Source: Journal of Investigative Medicine : the Official Publication of the American Federation for Clinical Research. 2002 March; 50(2): 95-100. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11928948&dopt=Abstract

- **Nontraumatic subcutaneous emphysema.**
  Author(s): Anand A.
  Source: Journal of Pain and Symptom Management. 2000 September; 20(3): 159-60.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11183732&dopt=Abstract

- **Normal diffusing capacity in patients with PiZ alpha(1)-antitrypsin deficiency, severe airflow obstruction, and significant radiographic emphysema.**
  Author(s): Wilson JS, Galvin JR.
  Source: Chest. 2000 September; 118(3): 867-71.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10988219&dopt=Abstract

- **Nutritional status and muscle strength in patients with emphysema and severe alpha(1)-antitrypsin deficiency.**
  Author(s): Piitulainen E, Areberg J, Linden M, Eriksson S, Mattsson S, Wollmer P.
  Source: Chest. 2002 October; 122(4): 1240-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12377848&dopt=Abstract

- **One-sided high-frequency oscillatory ventilation in the management of an acquired neonatal lobar emphysema: a case report and review.**
  Author(s): Andreou A, Papouli M, Netskos D, Papadopoulou F, Rossiou E.
  Source: Journal of Perinatology : Official Journal of the California Perinatal Association. 2001 January-February; 21(1): 61-4. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11268869&dopt=Abstract

- **Orbital emphysema and diplopia following thoracotomy.**
  Author(s): Fox RJ, Teener JW, Liu GT.
  Source: Eur J Ophthalmol. 1999 October-December; 9(4): 309-11.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10651196&dopt=Abstract

- **Orbital emphysema during air travel: a case report.**
  Author(s): Monaghan AM, Millar BG.
  Source: Journal of Cranio-Maxillo-Facial Surgery : Official Publication of the European Association for Cranio-Maxillo-Facial Surgery. 2002 December; 30(6): 367-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12425992&dopt=Abstract

- **Outcome after unilateral lung volume reduction surgery in patients with severe emphysema.**
  Author(s): Geiser T, Schwizer B, Krueger T, Gugger M, Hof VI, Dusmet M, Fitting JW, Ris HB.
  Source: European Journal of Cardio-Thoracic Surgery : Official Journal of the European Association for Cardio-Thoracic Surgery. 2001 October; 20(4): 674-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11574206&dopt=Abstract

- **Outcome of bilateral lung volume reduction in patients with emphysema potentially eligible for lung transplantation.**
  Author(s): Meyers BF, Yusen RD, Guthrie TJ, Davis G, Pohl MS, Lefrak SS, Patterson GA, Cooper JD.
  Source: The Journal of Thoracic and Cardiovascular Surgery. 2001 July; 122(1): 10-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11436031&dopt=Abstract

- **Overestimated frequency of a possible emphysema-susceptibility allele when microsomal epoxide hydrolase is genotyped by the conventional polymerase chain reaction-based method.**
  Author(s): Keicho N, Emi M, Kajita M, Matsushita I, Nakata K, Azuma A, Ohishi N, Kudoh S.
  Source: Journal of Human Genetics. 2001; 46(2): 96-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11281420&dopt=Abstract

- **Oxidative mechanisms in tobacco smoke-induced emphysema.**
  Author(s): Seagrave J.
  Source: Journal of Toxicology and Environmental Health. Part A. 2000 September 15; 61(1): 69-78. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10990164&dopt=Abstract

- **Pathogenesis and management of virus infection-induced exacerbation of senile bronchial asthma and chronic pulmonary emphysema.**
  Author(s): Yamaya M.
  Source: The Tohoku Journal of Experimental Medicine. 2002 June; 197(2): 67-80. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12233786&dopt=Abstract

- **Pathologic quiz case: patient with chronic obstructive pulmonary disease. Diffuse pulmonary neuroendocrine hyperplasia with multifocal tumorlets, immunoreactive to synaptophysin, associated with pulmonary emphysema.**
  Author(s): Dahiya M, Husain AN.
  Source: Archives of Pathology & Laboratory Medicine. 2000 January; 124(1): 171-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10629157&dopt=Abstract

- **Pathological case of the month. Persistent interstitial pulmonary emphysema presenting as a large unilocular cyst in an asymptomatic infant.**
  Author(s): Drut R, Drut M.
  Source: Archives of Pediatrics & Adolescent Medicine. 2000 January; 154(1): 87-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10632259&dopt=Abstract

- **Paying the piper: the NETT strikes a sour note. National Emphysema Treatment Trial.**
  Author(s): Cooper JD.
  Source: The Annals of Thoracic Surgery. 2001 August; 72(2): 330-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11515861&dopt=Abstract

- **Percutaneous drainage and/or nephrectomy in the treatment of emphysematous pyelonephritis.**
  Author(s): Mydlo JH, Maybee GJ, Ali-Khan MM.
  Source: Urologia Internationalis. 2003; 70(3): 147-50. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12660447&dopt=Abstract

- **Persistent pulmonary interstitial emphysema in an unventilated neonate.**
  Author(s): Gurakan B, Tarcan A, Arda IS, Coskun M.
  Source: Pediatric Pulmonology. 2002 November; 34(5): 409-11.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12357492&dopt=Abstract

- **Pictorial CME. Emphysematous pyelonephritis.**
  Author(s): Raj RS, Deepak S, Bronson SG, Sibi, Joseph W, Thomas M.
  Source: J Assoc Physicians India. 2002 September; 50: 1162. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12516701&dopt=Abstract

- **Pneumomediastinum and cervical emphysema associated with unusual clinical and electrocardiographic manifestations--a case report.**
  Author(s): Kounis NG, Zavras GM, Papadaki PJ, Kouni SN, Batsolaki M, Gouvelou-Deligianni GV, Koutsojannis CC.
  Source: Angiology. 2003 September-October; 54(5): 631-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14565642&dopt=Abstract

- **Pneumomediastinum and subcutaneous emphysema in an 18-month-old child.**
  Author(s): Gesundheit B, Preminger A, Harito B, Babyn P, Maayan C, Mei-Zahav M.
  Source: The Journal of Pediatrics. 2002 July; 141(1): 116-20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12091861&dopt=Abstract

- **Pneumomediastinum and subcutaneous emphysema--unusual complications of automated peritoneal dialysis.**
  Author(s): Zbroch E, Malyszko J, Kamocki Z, Mysliwiec M.
  Source: Perit Dial Int. 2003 January-February; 23(1): 97-8. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12691520&dopt=Abstract

- **Pneumomediastinum, pneumothorax and subcutaneous emphysema complicating MIS herniorrhaphy.**
  Author(s): Browne J, Murphy D, Shorten G.
  Source: Canadian Journal of Anaesthesia = Journal Canadien D'anesthesie. 2000 January; 47(1): 69-72.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10626724&dopt=Abstract

- **Pneumoretroperitoneum, pneumomediastinum, pneumopericardium, and subcutaneous emphysema complicating sigmoidoscopy: report of a case.**
  Author(s): Ota H, Fujita S, Nakamura T, Tanaka S, Tono T, Murata Y, Tanaka N, Okajima S.
  Source: Surgery Today. 2003; 33(4): 305-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12707830&dopt=Abstract

- **Pneumothorax with soft tissue emphysema following abrupt wake-up and self-extubation.**
  Author(s): Maestrello CL, Campbell RL, Campbell JR.
  Source: Anesthesia Progress. 2001 Winter; 48(1): 27-31.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11495402&dopt=Abstract

- **Polymers of alpha(1)-antitrypsin are chemotactic for human neutrophils: a new paradigm for the pathogenesis of emphysema.**
  Author(s): Parmar JS, Mahadeva R, Reed BJ, Farahi N, Cadwallader KA, Keogan MT, Bilton D, Chilvers ER, Lomas DA.
  Source: American Journal of Respiratory Cell and Molecular Biology. 2002 June; 26(6): 723-30.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12034572&dopt=Abstract

- **Post-measles pneumomediastinum and subcutaneous emphysema in malnourished children.**
  Author(s): Swar MO, Srikrishna BV, Abusin A, Khogali FM.
  Source: Afr J Med Med Sci. 2002 September; 31(3): 259-61.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12751568&dopt=Abstract

- **Post-operative surgical emphysema following the use of a peak flow meter.**
  Author(s): Oliver R, Coulthard P.
  Source: The British Journal of Oral & Maxillofacial Surgery. 2002 October; 40(5): 452-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12379200&dopt=Abstract

- **Predominant emphysema phenotype in chronic obstructive pulmonary.**
  Author(s): Boschetto P, Miniati M, Miotto D, Braccioni F, De Rosa E, Bononi I, Papi A, Saetta M, Fabbri LM, Mapp CE.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2003 March; 21(3): 450-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12662000&dopt=Abstract

- **Primary lung carcinoma arising from emphysematous bullae.**
  Author(s): Hanaoka N, Tanaka F, Otake Y, Yanagihara K, Nakagawa T, Kawano Y, Miyahara R, Li M, Wada H.
  Source: Lung Cancer (Amsterdam, Netherlands). 2002 November; 38(2): 185-91.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12399131&dopt=Abstract

- **Progressive adult-onset emphysema in transgenic mice expressing human MMP-1 in the lung.**
  Author(s): Foronjy RF, Okada Y, Cole R, D'Armiento J.
  Source: American Journal of Physiology. Lung Cellular and Molecular Physiology. 2003 May; 284(5): L727-37. Epub 2003 January 10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12676763&dopt=Abstract

- **Pulmonary interstitial emphysema.**
  Author(s): Thoongsuwan N, Stern EJ.
  Source: Current Problems in Diagnostic Radiology. 2002 March-April; 31(2): 63-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12077574&dopt=Abstract

- **Quality of life before and after lung transplantation in patients with emphysema versus other indications.**
  Author(s): TenVergert EM, Vermeulen KM, Geertsma A, van Enckevort PJ, de Boer WJ, van der Bij W, Koeter GH.
  Source: Psychological Reports. 2001 December; 89(3): 707-17.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11824741&dopt=Abstract

- **Quantitative analysis of technegas SPECT: evaluation of regional severity of emphysema.**
  Author(s): Nagao M, Murase K, Ichiki T, Sakai S, Yasuhara Y, Ikezoe J.
  Source: Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine. 2000 April; 41(4): 590-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10768557&dopt=Abstract

- **Quantitative computed tomography assessment of lung structure and function in pulmonary emphysema.**
  Author(s): Madani A, Keyzer C, Gevenois PA.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2001 October; 18(4): 720-30. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11716178&dopt=Abstract

- **Radiographically occult congenital lobar emphysema presenting as unexplained neonatal tachypnea.**
  Author(s): Rusakow LS, Khare S.
  Source: Pediatric Pulmonology. 2001 September; 32(3): 246-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11536454&dopt=Abstract

- **Radiologic assessment of emphysema for lung volume reduction surgery.**
  Author(s): Gierada DS.
  Source: Semin Thorac Cardiovasc Surg. 2002 October; 14(4): 381-90. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12652443&dopt=Abstract

- **Rapunzel syndrome causing gastric emphysema and small bowel obstruction.**
  Author(s): Klipfel AA, Kessler E, Schein M.
  Source: Surgery. 2003 January; 133(1): 120-1.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12563250&dopt=Abstract

- **Recent advances in diagnosis and management of chronic bronchitis and emphysema.**
  Author(s): Chitkara RK, Sarinas PS.
  Source: Current Opinion in Pulmonary Medicine. 2002 March; 8(2): 126-36. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11845008&dopt=Abstract

- **Reduction pneumoplasty for severe emphysema. Does the debate await a neat sentence?**
  Author(s): Mineo TC, Pompeo E.
  Source: Minerva Chir. 2002 October; 57(5): 625-33. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12370663&dopt=Abstract

- **Reduction pneumoplasty versus respiratory rehabilitation in severe emphysema: a randomized study. Pulmonary Emphysema Research Group.**
  Author(s): Pompeo E, Marino M, Nofroni I, Matteucci G, Mineo TC.
  Source: The Annals of Thoracic Surgery. 2000 September; 70(3): 948-53; Discussion 954.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11016339&dopt=Abstract

- **Relationship between extent of pulmonary emphysema by high-resolution computed tomography and lung elastic recoil in patients with chronic obstructive pulmonary disease.**
  Author(s): Baldi S, Miniati M, Bellina CR, Battolla L, Catapano G, Begliomini E, Giustini D, Giuntini C.
  Source: American Journal of Respiratory and Critical Care Medicine. 2001 August 15; 164(4): 585-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11520720&dopt=Abstract

- **Relationship between lung function, ventilation-perfusion inequality and extent of emphysema as assessed by high-resolution computed tomography.**
  Author(s): Sandek K, Bratel T, Lagerstrand L, Rosell H.
  Source: Respiratory Medicine. 2002 November; 96(11): 934-43.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12418592&dopt=Abstract

- **Relationship between regional severity of emphysema and coronary heart disease.**
  Author(s): Nagao M, Murase K, Ichiki T, Sakai S, Yasuhara Y, Ikezoe J.
  Source: Ann Nucl Med. 2000 October; 14(5): 369-72.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11108166&dopt=Abstract

- **Relief of tension subcutaneous emphysema with a small-bore subcutaneous drain.**
  Author(s): Thomas MJ, Mal R.
  Source: Anaesthesia. 2001 June; 56(6): 593-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11412183&dopt=Abstract

- **Renal scan in emphysematous pyelitis.**
  Author(s): Solav S, Date J, Shinde S.
  Source: Clinical Nuclear Medicine. 2001 December; 26(12): 1043.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11711715&dopt=Abstract

- **Repeatability of lung density measurements with low-dose computed tomography in subjects with alpha-1-antitrypsin deficiency-associated emphysema.**
  Author(s): Stolk J, Dirksen A, van der Lugt AA, Hutsebaut J, Mathieu J, de Ree J, Reiber JH, Stoel BC.
  Source: Investigative Radiology. 2001 November; 36(11): 648-51.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11606842&dopt=Abstract

- **Repeatability of quantitative CT indexes of emphysema in patients evaluated for lung volume reduction surgery.**
  Author(s): Gierada DS, Yusen RD, Pilgram TK, Crouch L, Slone RM, Bae KT, Lefrak SS, Cooper JD.
  Source: Radiology. 2001 August; 220(2): 448-54.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11477250&dopt=Abstract

- **Reproducibility of scoring emphysema by HRCT.**
  Author(s): Malinen A, Erkinjuntti-Pekkanen R, Partanen K, Rytkonen H, Vanninen R.
  Source: Acta Radiologica (Stockholm, Sweden : 1987). 2002 January; 43(1): 54-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11972463&dopt=Abstract

- **Residents' corner. Answer to case of the month #86. Emphysematous gastritis.**
  Author(s): Ho DC, Moore LA, Downey DB.
  Source: Canadian Association of Radiologists Journal = Journal L'association Canadienne Des Radiologistes. 2002 December; 53(5): 309-11.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12500386&dopt=Abstract

- **Respiratory system mechanics in a patient with massive subcutaneous emphysema.**
  Author(s): Parker AL, McCool FD.
  Source: Medicine and Health, Rhode Island. 2001 November; 84(11): 369-71.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12355665&dopt=Abstract

- **Response of whole-body protein and urea turnover to exercise differs between patients with chronic obstructive pulmonary disease with and without emphysema.**
  Author(s): Engelen MP, Deutz NE, Mostert R, Wouters EF, Schols AM.
  Source: The American Journal of Clinical Nutrition. 2003 April; 77(4): 868-74.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12663285&dopt=Abstract

- **Roger S. Mitchell lecture. Uses of expression microarrays in studies of pulmonary fibrosis, asthma, acute lung injury, and emphysema.**
  Author(s): Sheppard D.
  Source: Chest. 2002 March; 121(3 Suppl): 21S-25S.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11893658&dopt=Abstract

- **Role of secretory leukocyte protease inhibitor in the development of subclinical emphysema.**
  Author(s): Betsuyaku T, Takeyabu K, Tanino M, Nishimura M.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2002 June; 19(6): 1051-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12108856&dopt=Abstract

- **Ruptured mycotic aneurysm of the iliac artery complicated by emphysematous psoas muscle abscess: report of two cases.**
  Author(s): Chen CW, Ko WC, Sung JM, Huang JJ.
  Source: J Formos Med Assoc. 2002 February; 101(2): 144-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12099206&dopt=Abstract

- **Severe exertional dyspnea in a patient with localized emphysema.**
  Author(s): Giustino G, Webb KA, Sutherland KB, O'Donnell DE.
  Source: Can Respir J. 1999 November-December; 6(6): 535-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10623791&dopt=Abstract

- **Significance of pulmonary artery pressure in emphysema patients with mild-to-moderate hypoxemia.**
  Author(s): Doi M, Nakano K, Hiramoto T, Kohno N.
  Source: Respiratory Medicine. 2003 August; 97(8): 915-20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12924518&dopt=Abstract

- **Single-breath diffusing capacity of the lung for carbon monoxide: a predictor of PaO2, maximum work rate, and walking distance in patients with emphysema.**
  Author(s): Mohsenifar Z, Lee SM, Diaz P, Criner G, Sciurba F, Ginsburg M, Wise RA.
  Source: Chest. 2003 May; 123(5): 1394-400.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12740253&dopt=Abstract

- **Sonographic detection of emphysematous cystitis.**
  Author(s): Choong KK.
  Source: Journal of Ultrasound in Medicine : Official Journal of the American Institute of Ultrasound in Medicine. 2003 August; 22(8): 847-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12901415&dopt=Abstract

- **Study on the usefulness of seratrodast in the treatment of chronic pulmonary emphysema.**
  Author(s): Horiguchi T, Tachikawa S, Kondo R, Shiga M, Hirose M, Fukumoto K.
  Source: Arzneimittel-Forschung. 2002; 52(10): 764-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12442639&dopt=Abstract

- **Subcutaneous emphysema in a pediatric patient after radiologic placement of a percutaneous gastrostomy tube.**
  Author(s): Bernstein S, Weinstein M, Connolly B, Temple M.
  Source: Ajr. American Journal of Roentgenology. 2001 September; 177(3): 693-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11517077&dopt=Abstract

- **Subcutaneous emphysema secondary to foreign-body aspiration.**
  Author(s): Findlay CA, Morrissey S, Paton JY.
  Source: Pediatric Pulmonology. 2003 July; 36(1): 81-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12772230&dopt=Abstract

- **Subcutaneous emphysema secondary to tonsillectomy: a case report.**
  Author(s): Nishino H, Kenmochi M, Kasugai S, Okada T, Ohashi T.
  Source: Auris, Nasus, Larynx. 2003 February; 30 Suppl: S135-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12543179&dopt=Abstract

- **Subcutaneous leak with subcutaneous emphysema following PEG.**
  Author(s): Yusoff IF, Ormonde DG.
  Source: Gastrointestinal Endoscopy. 2000 January; 51(1): 88-90.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10625808&dopt=Abstract

- **Surgery for emphysema.**
  Author(s): Mintz J.
  Source: The New England Journal of Medicine. 2002 March 14; 346(11): 860-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11898810&dopt=Abstract

- **Surgery for emphysema.**
  Author(s): Dillard LS.
  Source: The New England Journal of Medicine. 2002 March 14; 346(11): 860-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11898809&dopt=Abstract

- **Surgery for emphysema.**
  Author(s): Meyers FJ.
  Source: The New England Journal of Medicine. 2002 March 14; 346(11): 860-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11898808&dopt=Abstract

- **Surgery for emphysema.**
  Author(s): Cooper JD, Lefrak SS.
  Source: The New England Journal of Medicine. 2002 March 14; 346(11): 860-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11893802&dopt=Abstract

- **Surgical emphysema and Collet-Sicard syndrome after cryoblockade of the inferior alveolar nerve.**
  Author(s): Willy PJ, McArdle P, Peters WJ.
  Source: The British Journal of Oral & Maxillofacial Surgery. 2003 June; 41(3): 190-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12804546&dopt=Abstract

- **Surgical emphysema following intraoral drainage of buccal space abscess.**
  Author(s): Srirompotong S, Srirompotong S.
  Source: J Med Assoc Thai. 2002 December; 85(12): 1314-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12678170&dopt=Abstract

- **Surgical emphysema following nose blowing.**
  Author(s): Dunn C.
  Source: The Journal of Laryngology and Otology. 2003 February; 117(2): 141-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12625891&dopt=Abstract

- **Surgical emphysema following routine preparation.**
  Author(s): Chapman DJ.
  Source: British Dental Journal. 2002 October 26; 193(8): 429.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12516667&dopt=Abstract

- **Surgical emphysema of the scrotum--another complication of ERCP?**
  Author(s): Laosebikan AO, Thomson SR, Ghimenton F, Campbell HT.
  Source: South African Medical Journal. Suid-Afrikaanse Tydskrif Vir Geneeskunde. 2003 July; 93(7): 504-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12939919&dopt=Abstract

- **Surgical emphysema over the pelvis: an unusual physical sign found on primary survey.**
  Author(s): Lim J, Porter KM.
  Source: Emergency Medicine Journal : Emj. 2002 March; 19(2): 180-1.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11904278&dopt=Abstract

- **Surgical treatment for patients with lung cancer complicated by severe pulmonary emphysema.**
  Author(s): Hayashi K, Fukushima K, Sagara Y, Takeshita M.
  Source: Jpn J Thorac Cardiovasc Surg. 1999 December; 47(12): 583-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10658374&dopt=Abstract

- **The correlation of emphysema or airway obstruction with the risk of lung cancer: a matched case-controlled study.**
  Author(s): Kishi K, Gurney JW, Schroeder DR, Scanlon PD, Swensen SJ, Jett JR.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2002 June; 19(6): 1093-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12108862&dopt=Abstract

- **The development of subcutaneous emphysema after delivery on a specially designed chair.**
  Author(s): Tjalma WA, Eelen CM.
  Source: Clin Exp Obstet Gynecol. 2002; 29(1): 22.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12013084&dopt=Abstract

- **The National Emphysema Treatment Trial: a paradigm for future surgical trials.**
  Author(s): Wood DE, DeCamp MM.
  Source: The Annals of Thoracic Surgery. 2001 August; 72(2): 327-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11515860&dopt=Abstract

- **The National Emphysema Treatment Trial--how strong is the evidence?**
  Author(s): Ware JH.
  Source: The New England Journal of Medicine. 2003 May 22; 348(21): 2055-6. Epub 2003 May 20.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12759478&dopt=Abstract

- **The outcome of volume reduction surgery according to the underlying type of emphysema.**
  Author(s): Sugi K, Kaneda Y, Murakami T, Esato K.
  Source: Surgery Today. 2001; 31(7): 580-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11495151&dopt=Abstract

- **The pathobiological mechanisms of emphysema models: what do they have in common?**
  Author(s): Tuder RM, McGrath S, Neptune E.
  Source: Pulmonary Pharmacology & Therapeutics. 2003; 16(2): 67-78. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12670776&dopt=Abstract

- **The ratio of the alveolar ventilations of SF6 and He in patients with lung emphysema and in healthy subjects.**
  Author(s): Luijendijk SC, van der Grinten CP.
  Source: Respiratory Physiology & Neurobiology. 2002 March; 130(1): 69-77.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12380017&dopt=Abstract

- **The relation of body mass index to asthma, chronic bronchitis, and emphysema.**
  Author(s): Guerra S, Sherrill DL, Bobadilla A, Martinez FD, Barbee RA.
  Source: Chest. 2002 October; 122(4): 1256-63.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12377850&dopt=Abstract

- **The role of collagenase in emphysema.**
  Author(s): Foronjy R, D'Armiento J.
  Source: Respiratory Research. 2001; 2(6): 348-52. Epub 2001 September 19. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11737934&dopt=Abstract

- **The UPAO test in preoperative evaluation for major pulmonary resection: an operative case with markedly improved ventilatory function after radical pulmonary resection for lung cancer associated with pulmonary emphysema.**
  Author(s): Hayashi A, Takamori S, Mitsuoka M, Miwa K, Fukunaga M, Matono K, Shirouzu K.
  Source: Ann Thorac Cardiovasc Surg. 2002 June; 8(3): 154-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12472398&dopt=Abstract

- **The use of nebulized glutathione in the treatment of emphysema: a case report.**
  Author(s): Lamson DW, Brignall MS.
  Source: Alternative Medicine Review : a Journal of Clinical Therapeutic. 2000 October; 5(5): 429-31.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11056412&dopt=Abstract

- **The use of pulmonary interstitial emphysema as an indicator of live birth.**
  Author(s): Lavezzi WA, Keough KM, Der'Ohannesian P, Person TL, Wolf BC.
  Source: The American Journal of Forensic Medicine and Pathology : Official Publication of the National Association of Medical Examiners. 2003 March; 24(1): 87-91.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12605006&dopt=Abstract

- **Thirteen-year experience in lung transplantation for emphysema.**
  Author(s): Cassivi SD, Meyers BF, Battafarano RJ, Guthrie TJ, Trulock EP, Lynch JP, Cooper JD, Patterson GA.
  Source: The Annals of Thoracic Surgery. 2002 November; 74(5): 1663-9; Discussion 1669-70.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12440627&dopt=Abstract

- **Thoracoscopic lung volume reduction surgery for pulmonary emphysema patients with severe hypercapnia.**
  Author(s): Mitsui K, Kurokawa Y, Kaiwa Y, Ando K, Kurosawa H, Hida W, Satomi S.
  Source: Jpn J Thorac Cardiovasc Surg. 2001 August; 49(8): 481-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11552273&dopt=Abstract

- **Thoracoscopic view of subcutaneous and subpleural emphysema.**
  Author(s): van Herreweghe R, Noppen M, Meysman M, Vincken W.
  Source: Respiration; International Review of Thoracic Diseases. 2002; 69(6): 542.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12457008&dopt=Abstract

- **Tracheal necrosis and surgical emphysema: a rare complication of thyroidectomy.**
  Author(s): To EW, Tsang WM, Williams MD, Lai EC, Chan M.
  Source: Ear, Nose, & Throat Journal. 2002 October; 81(10): 738-41.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12405096&dopt=Abstract

- **Transient exit block of a DDD pacemaker with unipolar leads in subcutaneous emphysema following pneumothorax.**
  Author(s): Melzer C, Witte HJ, Bauman G, Theres H.
  Source: Pacing and Clinical Electrophysiology : Pace. 2001 May; 24(5): 893-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11388111&dopt=Abstract

- **Traumatic retropharyngeal emphysema as a cause for severe respiratory distress in a newborn.**
  Author(s): Barlev DM, Nagourney BA, Saintonge R.
  Source: Pediatric Radiology. 2003 June; 33(6): 429-32. Epub 2003 March 04.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12768256&dopt=Abstract

- **Treatment of patients with lung cancer and severe emphysema: lessons from lung volume reduction surgery.**
  Author(s): Waddell TK.
  Source: Surgical Oncology. 2002 December; 11(4): 201-6. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12450556&dopt=Abstract

- **Tumour necrosis factor family genes in a phenotype of COPD associated with emphysema.**
  Author(s): Ferrarotti I, Zorzetto M, Beccaria M, Gile LS, Porta R, Ambrosino N, Pignatti PF, Cerveri I, Pozzi E, Luisetti M.
  Source: The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology. 2003 March; 21(3): 444-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12661999&dopt=Abstract

- **Unilateral pulmonary interstitial emphysema following pneumonia in a preterm infant successfully treated with prolonged selective bronchial intubation.**
  Author(s): O'Donovan D, Wearden M, Adams J.
  Source: American Journal of Perinatology. 1999; 16(7): 327-31.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10614699&dopt=Abstract

- **Unsuspected pseudophysiologic emphysema in chronic persistent asthma.**
  Author(s): Gelb AF, Zamel N.
  Source: American Journal of Respiratory and Critical Care Medicine. 2000 November; 162(5): 1778-82.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11069812&dopt=Abstract

- **Urinary desmosine excretion is inversely correlated with the extent of emphysema in patients with chronic obstructive pulmonary disease.**
  Author(s): Cocci F, Miniati M, Monti S, Cavarra E, Gambelli F, Battolla L, Lucattelli M, Lungarella G.
  Source: The International Journal of Biochemistry & Cell Biology. 2002 June; 34(6): 594-604.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11943590&dopt=Abstract

- **Usefulness of the double-wall sign in detecting pneumothorax in patients with giant bullous emphysema.**
  Author(s): Waitches GM, Stern EJ, Dubinsky TJ.
  Source: Ajr. American Journal of Roentgenology. 2000 June; 174(6): 1765-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10845520&dopt=Abstract

- **Vaginitis emphysematosa.**
  Author(s): Al Aboud K, Al Hawsawi K, Ramesh V.
  Source: Sexually Transmitted Infections. 2002 April; 78(2): 155.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12081185&dopt=Abstract

- **Vaginitis emphysematosa: CT and review of the literature.**
  Author(s): Leder RA, Paulson EK.
  Source: Ajr. American Journal of Roentgenology. 2001 March; 176(3): 623-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11222191&dopt=Abstract

- **Vascular atrophy and VEGFR-2 signaling: old theories of pulmonary emphysema meet new data.**
  Author(s): Shapiro SD.
  Source: The Journal of Clinical Investigation. 2000 December; 106(11): 1309-10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11104783&dopt=Abstract

- **Vascular endothelial growth factor and the pathogenesis of emphysema.**
  Author(s): Wagner PD.
  Source: The American Journal of Medicine. 2003 April 1; 114(5): 413-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12714134&dopt=Abstract

- **Visual classification of emphysema heterogeneity compared with objective measurements: HRCT vs spiral CT in candidates for lung volume reduction surgery.**
  Author(s): Cederlund K, Bergstrand L, Hogberg S, Rasmussen E, Svane B, Tylen U, Aspelin P.
  Source: European Radiology. 2002 May; 12(5): 1045-51. Epub 2002 January 26.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11976845&dopt=Abstract

- **Visual grading of emphysema severity in candidates for lung volume reduction surgery. Comparison between HRCT, spiral CT and "density-masked" images.**
  Author(s): Cederlund K, Bergstrand L, Hogberg S, Rasmussen E, Svane B, Aspelin P.
  Source: Acta Radiologica (Stockholm, Sweden : 1987). 2002 January; 43(1): 48-53.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11972462&dopt=Abstract

- **Volume displaced by diaphragm motion in emphysema.**
  Author(s): Singh B, Eastwood PR, Finucane KE.
  Source: Journal of Applied Physiology (Bethesda, Md. : 1985). 2001 November; 91(5): 1913-23.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11641325&dopt=Abstract

CHAPTER 2. NUTRITION AND EMPHYSEMA

Overview

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

Finding Nutrition Studies on Emphysema

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 "emphysema" (or synonyms) into the search box, and click "Go." To narrow the search, you can also select the "Title" field.

---

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

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

- **(-)Epigallocatechin-3-gallate inhibits leukocyte elastase: potential of the phyto-factor in hindering inflammation, emphysema, and invasion.**
  Author(s): Department of Experimental Biomedical Sciences, Medical School of Padova, Italy.
  Source: Sartor, Luigi Pezzato, Elga Garbisa, Spiridione J-Leukoc-Biol. 2002 January; 71(1): 73-9 0741-5400
- **A pilot study of all-trans-retinoic acid for the treatment of human emphysema.**
  Author(s): Pulmonary and Critical Care Medicine, UCLA School of Medicine, Los Angeles, CA 99095-1690, USA.
  Source: Mao, Jenny T Goldin, Jonathan G Dermand, John Ibrahim, Grace Brown, Mathew S Emerick, Aletha McNitt Gray, Michael F Gjertson, David W Estrada, Francine Tashkin, Donald P Roth, Michael D Am-J-Respir-Crit-Care-Med. 2002 March 1; 165(5): 718-23 1073-449X
- **Acute pulmonary edema and emphysema in steers fed Old-World bluestem hay.**
  Source: Phillips, W.A. Von Tungeln, D. Mod-Vet-Pract. Santa Barbara, Calif. : American Veterinary Publications. March 1986. volume 67 (3) page 252-253. 0362-8140
- **An automated method to assess the distribution of low attenuation areas on chest CT scans in chronic pulmonary emphysema patients.**
  Author(s): Department of Clinical Physiology, Kyoto University, Japan.
  Source: Sakai, N Mishima, M Nishimura, K Itoh, H Kuno, K Chest. 1994 November; 106(5): 1319-25 0012-3692
- **Antenatal presentation of a child with congenital lobar emphysema.**
  Author(s): Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville 32610-0294.
  Source: Richards, D S Langham, M R Dolson, L H J-Ultrasound-Med. 1992 April; 11(4): 165-8 0278-4297
- **Bilateral emphysematous pyelonephritis resolving to medical therapy.**
  Author(s): Intensive Care Unit, Middlemore Hospital, Auckland, New Zealand.
  Source: Nagappan, R Kletchko, S J-Intern-Med. 1992 July; 232(1): 77-80 0954-6820
- **Bronchial dysgenesis and lobar emphysema in an adult cat.**
  Author(s): Derry Animal Hospital, Derry, NH
  Source: LaRue, M.J. Garlick, D.S. Lamb, C.R. O'Callaghan, M.W. Journal-of-the-American-Veterinary-Medical-Association (USA). (1 October 1990). volume 197(7) page 886-888. cats respiratory diseases bronchi case studies genetic disorders age 0003-1488
- **Bronchoscopic volume reduction: a safe and effective alternative to surgical therapy for emphysema.**
  Author(s): Brigham and Women's Hospital, Department of Pulmonary and Critical Care Medicine, 75 Francis Street, Boston, MA 02115, USA. eingenito@partners.org
  Source: Ingenito, E P Reilly, J J Mentzer, S J Swanson, S J Vin, R Keuhn, H Berger, R L Hoffman, A Am-J-Respir-Crit-Care-Med. 2001 July 15; 164(2): 295-301 1073-449X
- **Carrageenan-induced pulmonary emphysema of rabbit.**
  Author(s): Department of Pathology, Osaka City University Medical School, Japan.
  Source: Mitsuhashi, T Kuwahara, H Ikura, Y Tohoku-J-Exp-Med. 1989 February; 157(2): 163-76 0040-8727

- **Changes of myocardial capillary density in progression of experimental lung emphysema.**
  Author(s): Department of Pathological Anatomy, Medical School of Bialystok, Poland.
  Source: Sulkowski, S Musiatowicz, B Sulkowska, M Sobaniec Lotowska, M Dziechiol, J Sulik, M Szynaka, B Exp-Toxicol-Pathol. 1996 January; 48(1): 19-28 0940-2993
- **Cigarette smoke inhibits the growth of lung fibroblasts from patients with pulmonary emphysema.**
  Author(s): Division of Respiratory Medicine, Department of Internal Medicine, Fukuoka University School of Medicine, Fukuoka, Japan.
  Source: Nobukuni, S Watanabe, K Inoue, J Wen, F Q Tamaru, N Yoshida, M Respirology. 2002 September; 7(3): 217-23 1323-7799
- **Clinical relevance summary: Collagen vs elastin in pathogenesis of emphysema; cellular origin of elastases; bronchiolitis vs emphysema as a cause of airflow obstruction.**
  Author(s): Boston Veterans Affairs Medical Center, Boston, MA 02130, USA.
  Source: Snider, G L Chest. 2000 May; 117(5 Suppl 1): 244S-6S 0012-3692
- **CT of emphysema.**
  Author(s): Department of Radiology, University of Colorado Health Sciences Center, Denver, USA. newellj@njc.org
  Source: Newell, John D Jr Radiol-Clin-North-Am. 2002 January; 40(1): 31-42, vii 0033-8389
- **Effect of ascorbic acid on hydroxyl radical generation by chemical, enzymatic and cellular systems. Importance for antioxidant prevention of pulmonary emphysema.**
  Author(s): Department of Pneumonology and Allergology, Medical Academy, Lodz, Poland.
  Source: Nowak, D Piasecka, G Antczak, A Pietras, T Biomed-Biochim-Acta. 1991; 50(3): 265-72 0232-766X
- **Environmental mineral particles correlated with smoking, emphysema and lung cancer.**
  Author(s): Institute of Occupational Health, Helsinki, Finland.
  Source: Kalliomaki, P L Taikina Aho, O Paakko, P Anttila, S Sivonen, S J Kalliomaki, K Exp-Pathol. 1989; 37(1-4): 103-7 0232-1513
- **Every breath you take. Preventing and treating emphysema.**
  Source: Lewis, C FDA-Consum. 1999 Mar-April; 33(2): 9-13 0362-1332
- **Induction of emphysematous lesions in rat lung by beta-D-xyloside, an inhibitor of proteoglycan synthesis.**
  Author(s): Department of Biochemistry, University of Nijmegen, The Netherlands.
  Source: van Kuppevelt, T H van de Lest, C H Versteeg, E M Dekhuijzen, P N Veerkamp, J H Am-J-Respir-Cell-Mol-Biol. 1997 January; 16(1): 75-84 1044-1549
- **Maternal nicotine exposure during gestation and lactation of rats induce microscopic emphysema in the offspring.**
  Author(s): Department of Physiological Sciences, University of the Western Cape, Bellville, South Africa. gmaritz@uwc.ac.za
  Source: Maritz, G S Exp-Lung-Res. 2002 Jul-August; 28(5): 391-403 0190-2148
- **Possible role of iron in the pathogenesis of pulmonary emphysema in rabbits.**
  Author(s): Medical Faculty, Belgrade (Yugoslavia). Institute of Pathophysiology

Source: Vucevic, D. Pesic, C. Djarmati, D. Djordjevic Denic, G. Acta-Veterinaria (Yugoslavia). (2001). volume 51(2-3) page 107-114. rabbits respiratory diseases iron pathogenesis 0567-8315

- **Recent advances in diagnosis and management of chronic bronchitis and emphysema.**
  Author(s): Division of Pulmonary, Critical Care, and Sleep Medicine, Veterans Administration Palo Alto Health Care System, and Stanford University School of Medicine, Palo Alto, California 94304, USA. rkc@stanford.edu
  Source: Chitkara, Rajinder K Sarinas, Priscilla S A Curr-Opin-Pulm-Med. 2002 March; 8(2): 126-36 1070-5287

- **Retinoids offer hope for the treatment of emphysema.**
  Author(s): m.giembycz@ic.ac.uk
  Source: Giembycz, M Trends-Pharmacol-Sci. 2000 August; 21(8): 292 0165-6147

- **Sequential targeted deficiency of SP-A and -D leads to progressive alveolar lipoproteinosis and emphysema.**
  Author(s): Cardiovascular Research Institute and Department of Pediatrics, University of California San Francisco, San Francisco, California 94118-1944, USA. hawgood@itsa.ucsf.edu
  Source: Hawgood, S Ochs, M Jung, A Akiyama, J Allen, L Brown, C Edmondson, J Levitt, S Carlson, E Gillespie, A M Villar, A Epstein, C J Poulain, F R Am-J-Physiol-Lung-Cell-Mol-Physiol. 2002 November; 283(5): L1002-10 1040-0605

- **Single breath N2 washout in papain-induced pulmonary emphysema.**
  Author(s): Klinik und Poliklinik fur Anasthesiologie und operative Intensivmedizin, Westfalischen Wilhelms-Universitat Munster, FRG.
  Source: Hachenberg, T Wendt, M Schreckenberg, U Meyer, J Hermeyer, G Muller, K M Lawin, P Intensive-Care-Med. 1989; 15(5): 308-13 0342-4642

- **Study on the usefulness of seratrodast in the treatment of chronic pulmonary emphysema.**
  Author(s): Department of Internal Medicine, Fujita Health University Second Hospital, Nagoya, Aichi, Japan. holiguchitakahiko@hotmail.com
  Source: Horiguchi, T Tachikawa, S Kondo, R Shiga, M Hirose, M Fukumoto, K Arzneimittelforschung. 2002; 52(10): 764-8 0004-4172

- **Sulfated polysaccharides prevent human leukocyte elastase-induced acute lung injury and emphysema in hamsters.**
  Author(s): Division of Pulmonary Medicine, University of Tennessee, Memphis.
  Source: Rao, N V Kennedy, T P Rao, G Ky, N Hoidal, J R Am-Rev-Respir-Dis. 1990 August; 142(2): 407-12 0003-0805

- **Synthetic serine elastase inhibitor reduces cigarette smoke-induced emphysema in guinea pigs.**
  Author(s): Department of Pathology, University of British Columbia, Vancouver, British Columbia, Canada. jlwright@interchange.ubc.ca
  Source: Wright, J L Farmer, S G Churg, A Am-J-Respir-Crit-Care-Med. 2002 October 1; 166(7): 954-60 1073-449X

- **The comparative study of reactive oxygen species generated by polymorphonuclear leukocytes as alpha 1-proteinase inhibitor inactivators-possible application for antioxidant prevention of emphysema.**
  Author(s): Clinic of Pneumonology and Allergology, Medical Academy, Lodz.
  Source: Nowak, D Arch-Immunol-Ther-Exp-(Warsz). 1988; 36(6): 723-31 0004-069X

- **The effect of high fat and high carbohydrate oral supplementation on nutritional status and respiratory function of six patients with emphysema.**
  Source: Hunt, K.L. Davies, M. Aust-j-nutr-diet. O'Connor, Australia : Dietitians Association of Australia. Sept 1993. volume 50 (3) page 93-97. 1032-1322
- **The relationship between selenium deficiency and the development of pulmonary and subcutaneous emphysema in bovine ephemeral fever virus-infected cattle.**
  Author(s): Department of Clinical Veterinary Studies, Faculty of Veterinary Science, University of Zimbabwe, Harare.
  Source: Odiawo, G O Onderstepoort-J-Vet-Res. 1989 June; 56(2): 123-5 0030-2465
- **Treatment of obstructive emphysema accompanied by edema with lung-ventilating and diuresis regimen--a dynamic observation of P (A-a) O2.**
  Source: Shao, C R Tang, Y X Fang, M Z Li, K N J-Tradit-Chin-Med. 1989 March; 9(1): 45-7 0254-6272
- **Ultrastructural analysis of pulmonary capillaries in the course of experimental lung emphysema.**
  Author(s): Department of Pathological Anatomy, Medical School, Bialystok.
  Source: Sulkowski, S Sulkowska, M Dzieciol, J Nowak, H F Pol-J-Pathol. 1996; 47(3): 135-40 1233-9687

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 emphysema; 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:

- **Minerals**

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

CHAPTER 3. ALTERNATIVE MEDICINE AND EMPHYSEMA

Overview

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

National Center for Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (**http://nccam.nih.gov/**) has created a link to the National Library of Medicine's databases to facilitate research for articles that specifically relate to emphysema 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 "emphysema" (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 emphysema:

- **(-)Epigallocatechin-3-gallate inhibits leukocyte elastase: potential of the phyto-factor in hindering inflammation, emphysema, and invasion.**
  Author(s): Sartor L, Pezzato E, Garbisa S.
  Source: Journal of Leukocyte Biology. 2002 January; 71(1): 73-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11781382&dopt=Abstract

- **Breathing exercises in the treatment of emphysema.**
  Author(s): Innocenti DM.
  Source: Physiotherapy. 1966 December; 52(12): 437-41. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5980343&dopt=Abstract

- **Breathing out into water during subtotal immersion: a therapy for chronic pulmonary emphysema.**
  Author(s): Kurabayashi H, Machida I, Tamura K, Iwai F, Tamura J, Kubota K.

Source: American Journal of Physical Medicine & Rehabilitation / Association of Academic Physiatrists. 2000 March-April; 79(2): 150-3.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10744189&dopt=Abstract

- **Breathing retraining. Mount Sinai Hospital emphysema-chronic bronchitis clinic.**
Author(s): Westreich N, Paguyo N, Cohen S, Grismer J.
Source: Minn Med. 1970 June; 53(6): 621-2. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5449271&dopt=Abstract

- **Care for emphysema and chronic bronchitis.**
Author(s): Petty TL, Neff TA.
Source: Annals of Internal Medicine. 1970 March; 72(3): 435-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5415427&dopt=Abstract

- **Chronic bronchial asthma and emphysema. Rehabilitation and use of thoracic vibrocompression.**
Author(s): Beck GJ.
Source: Geriatrics. 1966 June; 21(6): 139-58.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5936567&dopt=Abstract

- **Chronic bronchitis and emphysema.**
Author(s): Webster JR Jr, Addington WW.
Source: Postgraduate Medicine. 1971 December; 50(6): 113-8.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5128034&dopt=Abstract

- **Chronic obstructive emphysema.**
Author(s): Farber SM, Wilson RH.
Source: Clin Symp. 1968 April-June; 20(2): 35-69. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5742426&dopt=Abstract

- **Chronic obstructive pulmonary disease: current comprehensive care for emphysema and bronchitis.**
Author(s): Johannsen JM.
Source: The Nurse Practitioner. 1994 January; 19(1): 59-67. Review. Erratum In: Nurse Pract 1994 March; 19(3): 20.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8139803&dopt=Abstract

- **Clinical evaluation of 99mTc-Technegas SPECT in thoracoscopic lung volume reduction surgery in patients with pulmonary emphysema.**
Author(s): Inmai T, Sasaki Y, Shinkai T, Ohishi H, Nezu K, Nishimoto Y, Ichiba N, Yamane T, Yoshikawa M, Narita N, Uchida H.

Source: Ann Nucl Med. 2000 August; 14(4): 263-9.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11023026&dopt=Abstract

- **Coping with emphysema.**
Author(s): Barstow RE.
Source: Nurs Clin North Am. 1974 March; 9(1): 137-45. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4498703&dopt=Abstract

- **Editorial: Does treatment for severe emphysema and chronic bronchitis really help? (A response).**
Author(s): Petty TL.
Source: Chest. 1974 February; 65(2): 124-7.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4810668&dopt=Abstract

- **Effect of ascorbic acid on hydroxyl radical generation by chemical, enzymatic and cellular systems. Importance for antioxidant prevention of pulmonary emphysema.**
Author(s): Nowak D, Piasecka G, Antczak A, Pietras T.
Source: Biomed Biochim Acta. 1991; 50(3): 265-72.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1659390&dopt=Abstract

- **Effects of guided imagery in patients with chronic bronchitis and emphysema.**
Author(s): Moody LE, Fraser M, Yarandi H.
Source: Clinical Nursing Research. 1993 November; 2(4): 478-86.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8220200&dopt=Abstract

- **Effects of muscle relaxation therapy using specially designed plates in patients with pulmonary emphysema.**
Author(s): Fujimoto K, Kubo K, Miyahara T, Matsuzawa Y, Kobayashi T, Ono C, Ito N.
Source: Intern Med. 1996 October; 35(10): 756-63.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8933182&dopt=Abstract

- **Emphysema: incidence still rising, nursing care crucial.**
Author(s): Sweetwood H.
Source: Nursing. 1972 November; 2(11): 8-12.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4496327&dopt=Abstract

- **Experimental emphysema. Histologic changes and alterations in pulmonary circulation.**
Author(s): Brooksby GA, Dennis RL, Datnow B, Clark D.
Source: Calif Med. 1967 November; 107(5): 391-5. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6083243&dopt=Abstract

- **Experimental pulmonary emphysema in Syrian hamsters.**
  Author(s): Nakamura T, Ishikawa T, Niwa T, Ariji F, Matsuda T, Asoo N, Nagai H, Arai H, Yokosawa A, Sato H, Motomiya M, Konno K.
  Source: The Tohoku Journal of Experimental Medicine. 1976 December; 120(4): 319-27.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=827820&dopt=Abstract

- **Hyperbaric oxygenation as adjuvant therapy to surgery of emphysematous cholecystitis.**
  Author(s): Kraljevic D, Druzijanic N, Tomic I, Juricic J, Petri N.
  Source: Hepatogastroenterology. 1999 March-April; 46(26): 775-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10370610&dopt=Abstract

- **Imaging in the evaluation of emphysema.**
  Author(s): Robertson RJ.
  Source: Thorax. 1999 May; 54(5): 379.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10212098&dopt=Abstract

- **Improvement in ejection fraction by hydrotherapy as rehabilitation in patients with chronic pulmonary emphysema.**
  Author(s): Kurabayashi H, Machida I, Kubota K.
  Source: Physiotherapy Research International : the Journal for Researchers and Clinicians in Physical Therapy. 1998; 3(4): 284-91.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9859136&dopt=Abstract

- **Interactions of regional respiratory mechanics and pulmonary ventilatory impairment in pulmonary emphysema: assessment with dynamic MRI and xenon-133 single-photon emission CT.**
  Author(s): Suga K, Tsukuda T, Awaya H, Matsunaga N, Sugi K, Esato K.
  Source: Chest. 2000 June; 117(6): 1646-55.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10858397&dopt=Abstract

- **Lung volume reduction surgery for pulmonary emphysema using dynamic Xenon-133 and Tc-99m-MAA SPECT images.**
  Author(s): Sugi K, Matsuoka T, Tanaka T, Sakano H, Nawata K, Ueda K, Fujita N, Kaneda Y, Esato K.
  Source: Ann Thorac Cardiovasc Surg. 1998 June; 4(3): 149-53.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9660913&dopt=Abstract

- **Myofeedback: a new method of teaching breathing exercises in emphysematous patients.**
  Author(s): Johnston R, Lee K.

Source: Physical Therapy. 1976 July; 56(7): 826-31.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=132675&dopt=Abstract

- **Outpatient care for patients with chronic airway obstruction--emphysema and bronchitis.**
Author(s): Neff TA, Petty TL.
Source: Chest. 1971 August; 60(2): Suppl: 11S-17S.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5567449&dopt=Abstract

- **Preliminary application of dynamic pulmonary xenon-133 single-photon emission tomography in the evaluation of patients with pulmonary emphysema for thoracoscopic lung volume reduction surgery.**
Author(s): Suga K, Nishigauchi K, Matsunaga N, Matsumoto T, Kume N, Sugi K, Esato K.
Source: European Journal of Nuclear Medicine. 1998 April; 25(4): 410-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9553171&dopt=Abstract

- **Preoperative and postoperative imaging in the surgical management of pulmonary emphysema.**
Author(s): Slone RM, Gierada DS, Yusen RD.
Source: Radiologic Clinics of North America. 1998 January; 36(1): 57-89. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9465868&dopt=Abstract

- **Proposed study to evaluate the effect of osteopathic manipulative therapy in the treatment of the emphysema patient.**
Author(s): Foellner RP, Taylor RM, Marjan G, Kelso AF.
Source: J Am Osteopath Assoc. 1968 May; 67(9): 1075-6. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5185816&dopt=Abstract

- **Psychophysiologic predictors of weaning from mechanical ventilation in chronic bronchitis and emphysema.**
Author(s): Moody LE, Lowry L, Yarandi H, Voss A.
Source: Clinical Nursing Research. 1997 November; 6(4): 311-30; Discussion 330-3.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9384053&dopt=Abstract

- **Pulmonary emphysema. 2. Treatment of chronic pulmonary emphysema.**
Author(s): Miller WF.
Source: Postgraduate Medicine. 1966 March; 39(3): 230-9.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5905850&dopt=Abstract

- **Radiologic assessment of emphysema for lung volume reduction surgery.**
Author(s): Gierada DS.

Source: Semin Thorac Cardiovasc Surg. 2002 October; 14(4): 381-90. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12652443&dopt=Abstract

- **Radionuclide imaging in emphysema after lung volume reduction surgery.**
Author(s): Suga K, Nishigauchi K, Shimizu K, Kawamura T, Matsunaga N, Sugi K, Esato K.
Source: Clinical Nuclear Medicine. 1997 October; 22(10): 683-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9343723&dopt=Abstract

- **Respiration in emphysema patients.**
Author(s): Dirschel KM.
Source: Nurs Clin North Am. 1973 December; 8(4): 617-22. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4491055&dopt=Abstract

- **Reversal of electrocardiogram to normal in chronic obstructive pulmonary disease with emphysema.**
Author(s): Dines DE, Parkin TW.
Source: Archives of Internal Medicine. 1967 December; 120(6): 721-4.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4228639&dopt=Abstract

- **Spontaneous subcutaneous emphysema.**
Author(s): Balas P, Oeconomidis M, Tzamouranis D, Tripolitis A.
Source: American Journal of Surgery. 1974 June; 127(6): 755-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4832145&dopt=Abstract

- **The circulation in patients with chronic bronchitis and emphysema at rest and during exercise, with special reference to the influence of changes in blood viscosity and blood volume on the pulmonary circulation.**
Author(s): Segel N, Bishop JM.
Source: The Journal of Clinical Investigation. 1966 October; 45(10): 1555-68.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=5925514&dopt=Abstract

- **The effect of a pressurized environment (hyperbaric chamber) on pulmonary emphysema.**
Author(s): Chusid EL, Maher GG, Nicogossian A, Miller A, Teirstein A, Bader RA, Bader ME, Jacobson J 2nd.
Source: The American Journal of Medicine. 1972 December; 53(6): 743-7.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4634730&dopt=Abstract

- **The physiologic basis of training patients with emphysema.**
Author(s): Paez PN, Phillipson EA, Masangkay M, Sproule BJ.

Source: Am Rev Respir Dis. 1967 June; 95(6): 944-53. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6067380&dopt=Abstract

- **The rehabilitative program in pulmonary emphysema.**
  Author(s): Barach AL.
  Source: Journal of the American Geriatrics Society. 1967 February; 15(2): 183-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6017293&dopt=Abstract

- **The use of nebulized glutathione in the treatment of emphysema: a case report.**
  Author(s): Lamson DW, Brignall MS.
  Source: Alternative Medicine Review : a Journal of Clinical Therapeutic. 2000 October; 5(5): 429-31.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11056412&dopt=Abstract

- **Three-dimensional surface displays of perfusion SPET in the evaluation of patients with pulmonary emphysema for thoracoscopic lung volume reduction surgery.**
  Author(s): Suga K, Nishigauchi K, Matsunaga N, Kawakami Y, Kume N, Sugi K, Esato K.
  Source: Nuclear Medicine Communications. 1997 August; 18(8): 719-27.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9293502&dopt=Abstract

- **Treatment of obstructive emphysema accompanied by edema with lung-ventilating and diuresis regimen--a dynamic observation of P (A-a) O2.**
  Author(s): Shao CR, Tang YX, Fang MZ, Li KN.
  Source: J Tradit Chin Med. 1989 March; 9(1): 45-7. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2761283&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 emphysema; 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**

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

  Chronic Obstructive Pulmonary Disease
  Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

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

- **Alternative Therapy**

  Tai Chi
  Source: Integrative Medicine Communications; www.drkoop.com

- **Herbs and Supplements**

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

  Coltsfoot
  Alternative names: Tussilago farfara
  Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

Ipriflavone
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10039,00.html

N-Acetyl Cysteine (NAC)
Source: Prima Communications, Inc.www.personalhealthzone.com

Reverse Transcriptase Inhibitors
Source: Integrative Medicine Communications; www.drkoop.com

Valproic Acid Derivatives
Source: Integrative Medicine Communications; www.drkoop.com

General References

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

CHAPTER 4. DISSERTATIONS ON EMPHYSEMA

Overview

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

Dissertations on Emphysema

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 emphysema. You will see that the information provided includes the dissertation's title, its author, and the institution with which the author is associated. The following covers recent dissertations found when using this search procedure:

- **A Study of the Effect of a Pulmonary Rehabilitation Program on Anxiety, Medical Orientation, Social Introversion, Attitude toward Work, and Engagement in Vocational Activities in Patients with Chronic Obstructive Pulmonary Emphysema (COPD)** by Lustig, Felicia M., PhD from New York University, 1970, 124 pages
  http://wwwlib.umi.com/dissertations/fullcit/7026433
- **Locus-of-Control among Hospitalized Pulmonary Emphysema Patients.** by Ireland, Robert Ellis, PhD from University of Kansas, 1972, 162 pages
  http://wwwlib.umi.com/dissertations/fullcit/7311900
- **Marital Stress and Coping in Alpha 1-Antitrypsin Deficiency Emphysema** by Cannon, Christine Anna, PhD from University of Delaware, 1997, 264 pages
  http://wwwlib.umi.com/dissertations/fullcit/9718746
- **Probing Dynamic Lung Mechanical Properties in Emphysema and Asthmatic Patients** by Henderson, Angela Cortney; PhD from Boston University, 2003, 158 pages
  http://wwwlib.umi.com/dissertations/fullcit/3054528

- **The Singer's Breath: Implications for Treatment of Persons with Emphysema** by Engen, Rebecca Lynn; PhD from The University of Iowa, 2003, 189 pages
  http://wwwlib.umi.com/dissertations/fullcit/3087624

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 EMPHYSEMA

Overview

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

Recent Trials on Emphysema

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

- **Lung Volume Reductions Surgery (LVRS) Study**

  Condition(s): Emphysema

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Department of Veterans Affairs Medical Research Service

  Purpose - Excerpt: The main objectives of this study is to see if a type of lung surgery, known as lung reduction surgery, in addition to standard medical treatment improves the quality of life, lung function, and reduces the high mortality associated with severe **emphysema** when compared to standard medical treatment alone. Another goal of this study is to better identify the patients most likely to benefit from this surgical treatment. The information obtained in this study is important because lung reduction surgery is being done in several centers around the country but its long term benefits, if any, over standard medical treatment, are not known.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00018525

- **Study Evaluating the Safety and Efficacy of Infliximab in Subjects with Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD)**

  Condition(s): Pulmonary Disease, Chronic Obstructive; Chronic Bronchitis; Emphysema

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

Study Status: This study is currently recruiting patients.

Sponsor(s): Centocor

Purpose - Excerpt: The purpose of this study is to determine the safety and efficacy of infliximab in patients with moderate to severe Chronic Obstructive Pulmonary Disease.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00056264

- **To evaluate the long-term safety of (R,R)-formoterol in subjects with COPD**

  Condition(s): Chronic Obstructive Pulmonary Disease; Chronic Bronchitis; Emphysema

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Sepracor, Inc.

  Purpose - Excerpt: The purpose of this study is to determine the long-term safety of (R,R)-formoterol over a period of 12 months in subjects with COPD

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00064415

- **Yoga for Treating Shortness of Breath in Chronic Obstructive Pulmonary Disease (COPD)**

  Condition(s): Pulmonary Disease, Chronic Obstructive; Lung Diseases, Obstructive; Pulmonary Emphysema; Chronic Bronchitis

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Center for Complementary and Alternative Medicine (NCCAM)

  Purpose - Excerpt: The purpose of this study is to evaluate the safety and effectiveness of yoga in reducing shortness of breath in people with chronic obstructive pulmonary disease (COPD). Patients in this study must have moderate to severe COPD and be primarily limited by shortness of breath.

  Phase(s): Phase I; Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00051792

- **Determine the Safety and Efficacy of (R,R)-Formoterol in the Treatment of Subjects with COPD**

  Condition(s): Chronic Obstructive Pulmonary Disease; Chronic Bronchitis; Emphysema

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): Sepracor, Inc.

Purpose - Excerpt: The purpose of this study is to assess the bronchodilator effect and safety of multiple daily doses of (R,R)-formoterol administered for 12 weeks as maintenance treatment in patients with COPD

Phase(s): Phase III

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00064402

- **Efficacy of Osteopathic Manipulation in Chronic Obstructive Pulmonary Disease**

  Condition(s): Emphysema

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Center for Complementary and Alternative Medicine (NCCAM)

  Purpose - Excerpt: The purpose of this study is to determine if osteopathic manipulative treatment (OMT) is effective for persons with **emphysema** as a component of their chronic obstructive pulmonary disease.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00034112

- **Feasibility of Retinoic Acid Treatment in Emphysema (FORTE)**

  Condition(s): Emphysema; Lung Diseases; Lung Diseases, Obstructive; Chronic Obstructive Pulmonary Disease

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Heart, Lung, and Blood Institute (NHLBI)

  Purpose - Excerpt: To conduct feasibility studies on the use of retinoids in the treatment of emphysema. Specific objectives are to identify optimal patient populations, retinoids, doses, dosing schedules, routes of administration, and outcome measures preparatory to conducting a larger, controlled, clinical trial on the efficacy of retinoid therapy in the management of emphysema.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000621

- **National Emphysema Treatment Trial (NETT)**

  Condition(s): Emphysema; Lung Diseases; Lung Diseases, Obstructive; Chronic Obstructive Pulmonary Disease

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Heart, Lung, and Blood Institute (NHLBI)

  Purpose - Excerpt: To evaluate the long term efficacy, morbidity and mortality associated with medical therapy with lung volume reduction surgery (LVRS) as

compared to medical therapy alone and to define patient selection criteria. The trial, conducted in conjunction with a patient registry, is supported by the NHLBI, the Health Care Financing Administration (HCFA), and the Agency for Health Care Policy and Research (AHCPR).

Phase(s): Phase III

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00000606

- **Alpha1-antitrypsin Deficiency Registry**

  Condition(s): Lung Diseases; Emphysema; Alpha-1 antitrypsin deficiency; Chronic Obstructive Pulmonary Disease

  Study Status: This study is completed.

  Sponsor(s): National Heart, Lung, and Blood Institute (NHLBI)

  Purpose - Excerpt: To collect data from the 37 participating clinical centers on patients with alpha1-antitrypsin deficiency, including those who received replacement therapy with an intravenous preparation of alpha1-proteinase inhibitor (A1Pi) concentrate.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00005292

- **Characterization of the Pathobiology of Early Lung Destruction in Alpha 1-Antitrypsin Deficient Individuals**

  Condition(s): Emphysema; Lung Diseases, Obstructive; alpha 1-Antitrypsin Deficiency

  Study Status: This study is completed.

  Sponsor(s): National Heart, Lung, and Blood Institute (NHLBI)

  Purpose - Excerpt: Alpha 1-antitrypsin-deficient individuals develop severe destructive lung disease much earlier and their lung function declines faster than the general population of individuals with chronic obstructive lung disease. This study is designed to better understand the pathogenesis of lung destruction in alpha 1-antitrypsin deficient individuals and to characterize the pathobiology of early lung destruction. To accomplish this we intend to use bronchoalveolar lavage to determine and quantify the factors that initiate and sustain lung inflammation in alpha 1-antitrypsin deficient individuals with lung function above a force expiratory volume in one second (FEV1) of greater than 50% of predicted.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001462

- **Cost-Effectiveness of Lung Volume Reduction Surgery**

  Condition(s): Chronic Obstructive Pulmonary Disease; Emphysema

  Study Status: This study is completed.

Sponsor(s): Department of Veterans Affairs; Department of Veterans Affairs Health Services Research and Development Service

Purpose - Excerpt: Lung volume reduction surgery (LVRS) has been advanced as a therapy to significantly improve quality of life in patients with COPD, but to date no controlled studies have evaluated the impact of LVRS. Evaluate cost-effectiveness of LVRS compared to current therapy for COPD. This is a case control study in which veterans undergoing LVRS at VA Puget Sound Health Care System (VAPSHCS) are compared to patients with a similar severity of disease at Boise VAMC who are not undergoing LVRS. Changes in health related quality of life are being evaluated using three instruments: the SF-36, the St. George?s Respiratory Questionnaire, and the Quality of Well-Being Scale, the latter to calculate utility associated with different health states. Costs will be determined using utilization data on outpatient visits, medications, oxygen use, inpatient days, radiology tests, laboratory tests, and emergency room visits are being collected for the twelve months before and after surgery. Costs will be calculated according to VA and community standards.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00013156

- **Emphysema: Physiologic Effects of Nutritional Support**

  Condition(s): Emphysema; Lung Diseases; Lung Diseases, Obstructive; Chronic Obstructive Pulmonary Disease

  Study Status: This study is completed.

  Sponsor(s): National Heart, Lung, and Blood Institute (NHLBI)

  Purpose - Excerpt: To determine if enteral nutrition support (ENS) restores normal body weight and improves muscle strength, exercise performance, sensation of dyspnea, and quality of life in malnourished patients with chronic obstructive pulmonary disease.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000573

- **Honolulu Heart Program**

  Condition(s): Cardiovascular Diseases; Coronary Disease; Cerebrovascular Accident; Heart Diseases; Heart Failure, Congestive; Myocardial Infarction; Asthma; Emphysema; Lung Diseases, Obstructive; Aortic Aneurysm, Abdominal; Bronchitis; Dementia; Hypertension; Chronic Obstructive Pulmonary Disease; Heart Failure

  Study Status: This study is completed.

  Sponsor(s): National Heart, Lung, and Blood Institute (NHLBI)

  Purpose - Excerpt: To investigate coronary heart disease and stroke among American men of Japanese ancestry who were living on the island of Oahu in 1965. Morbidity and mortality surveillance of the original cohort is continuing.

  Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00005123

- **Medication Adherence in COPD--A Self-Regulation Study**

  Condition(s): Lung Diseases, Obstructive; Bronchitis; Emphysema; Chronic Obstructive Pulmonary Disease

  Study Status: This study is completed.

  Sponsor(s): National Heart, Lung, and Blood Institute (NHLBI)

  Purpose - Excerpt: To test the effectiveness of a self-management program for chronic obstructive disease (COPD) patients. The program to improve adherence could be conducted by nurses or other clinic staff in settings where comprehensive rehabilitation services were not available.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00005717

- **Tucson Epidemiology Study of Chronic Obstructive Lung Diseases**

  Condition(s): Asthma; Bronchitis; Emphysema; Lung Diseases, Obstructive; Chronic Obstructive Pulmonary Disease

  Study Status: This study is completed.

  Sponsor(s): National Heart, Lung, and Blood Institute (NHLBI)

  Purpose - Excerpt: To determine the natural history, etiology, and interrelationships of **emphysema,** chronic bronchitis, asthma, and related airways obstructive diseases. Also, to determine the relationship of acute lower respiratory tract illnesses in infants and children to the development of subsequent chronic lung disorders.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00005279

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 "emphysema" (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 EMPHYSEMA

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 "emphysema" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on emphysema, we have not necessarily excluded non-medical patents in this bibliography.

Patents on Emphysema

By performing a patent search focusing on emphysema, 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 emphysema:

- **Acylated enol derivatives as prodrugs of elastase inhibitors**

  Inventor(s): Burkhart; Joseph P. (West Chester, OH), Mehdi; Shujaath (West Chester, OH), Peet; Norton P. (Cincinnati, OH)

  Assignee(s): Merrell Pharmaceuticals Inc. (Bridgewater, NJ)

  Patent Number: 5,972,897

  Date filed: June 26, 1997

  Abstract: This invention relates to acylated enol derivatives of known elastase inhibitors. These compounds are useful in the treatment of various inflammatory diseases, including cystic fibrosis and **emphysema** or as prodrugs of compounds which are useful in the treatment of said diseases.

  Excerpt(s): This invention relates to compounds which are either elastase inhibitors or are prodrugs of elastase inhibitors, useful for a variety of physiological and end-use applications. Human neutrophil elastase has been implicated as an agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and rheumatoid arthritis. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of proteolytic activity against a number of connective tissue macromolecules including elastin, fibronectin, collagen, and proteoglycan. The presence of the enzyme elastase may contribute to the pathology of these diseases. Normal plasma contains large quantities of protease inhibitors that control a variety of enzymes involved in connective tissue turnover and inflammation. For example,.alpha.-1-proteinase inhibitor (.alpha.-1-PI) is a serine protease inhibitor that blocks the activity of elastase.alpha.-1-PI has received considerable interest because reduction in plasma levels to less than 15% of normal is associated with the early development of **emphysema.**

  Web site: http://www.delphion.com/details?pn=US05972897__

- **Analysis of predisposition based on human airway trypsin protease gene polymorphism**

  Inventor(s): Eguchi; Hiroshi (Tokyo, JP), Masuda; Kenichi (Tokyo, JP), Yamaoka; Kazuyoshi (Tokyo, JP), Yasuoka; Susumu (Tokushima, JP)

  Assignee(s): Teijin Limited (Osaka, JP)

  Patent Number: 6,346,385

  Date filed: June 15, 2000

  Abstract: A method for predicting the constitution susceptible to the onset of specific diseases in individual humans, for example, respiratory diseases such as chronic obstructive pulmonary diseases, sinobronchial syndrome, pulmonary **emphysema,** diffuse panbronchiolitis or bronchiectasis, effects of treatment on patients or prognosis of the treatment by analyzing the genetic polymorphisms of a human trypsin-like enzyme of the respiratory tract.

  Excerpt(s): This invention relates to a method for predicting the constitution susceptible to the onset of specific diseases, effects on methods of treatment for patients suffering

from said diseases or predicting the prognosis of the treatment by analysis of genetic polymorphisms of a human trypsin-like enzyme of a respiratory tract. Research on related genes has recently been promoted not only in genetic diseases due to deletion or mutation of single genes but also in multifactorial diseases caused by entanglement of several genetic predispositions and environmental factors. As a result, the deletion or point mutation and isoforms related to the multifactorial diseases and further mutation of genetic parts (introns or promoters) without affecting actually translated amino acid sequences have come to be considered as risk factors for the diseases. It has been published that the correlation is recognized between bone density and genetic polymorphisms of an intron of the vitamin D receptor in the osteopathic field as the prior art (Morrison, N. A. et al., Nature, 367: 284-287 1994). In the field of circulatory organs, it has been reported that the I type (insertion type) and D type (deletion type) genetic polymorphisms of an angiotensin-converting enzyme are associated with the onset of myocardial infarctions (Cambien, F. et al., Nature 359: 641-644, 1992) and the amino acid substitution of M295T of angiotensinogen and the polymorphisms of a promoter region of G-6A are associated with the onset of essential hypertension (Inoue, I. et al., J. Clin. Invest., 99: 1786-1797, 1997). Furthermore, in the field of the nervous system, it has been reported on the association between the onset of dementia and the isoforms of apoE protein. Much research has been carried out in the association between the genetic polymorphisms of glutathione S-transferase and the onset of cancers in the cancer-related field. As the field of respiratory diseases, it has been reported on the association between the onset or morbid state of asthma and the TNF (Moffatt, M. F. et al., Hum. Mol. Genet. 6 (4): 551-554, 1997) and the association between the onset or morbid state of the asthma and the genetic polymorphisms of an angiotensin converting enzyme (Benessiano, J. et al., J. Allergy Clin. Immunol. 99 (1): 53-57, 1997).

Web site: http://www.delphion.com/details?pn=US06346385__

- **Compounds**

  Inventor(s): Burgess; Nicola Anne (Edmonton, GB), Clinkenbeard; Helen Elizabeth (Hertford, GB), Southan; Christopher Donald (Bishop's Stortford, GB)

  Assignee(s): SmithKline Beecham p.l.c. (Middlesex, GB)

  Patent Number: 6,100,059

  Date filed: April 30, 1998

  Abstract: HGBAB90 polypeptides and polynucleotides and methods for producing such polypeptides by recombinant techniques are disclosed. Also disclosed are methods for utilizing HGBAB90 polypeptides and polynucleotides in the design of protocols for the treatment of pulmonary **emphysema,** arthritis, multiple sclerosis, periodontal disease, cystic fibrosis, respiratory disease, thrombosis, cancer, cachexia, angina, glaucoma, inflamatory disorders, osteoporosis, cardiovascular disorders such as hypertension, atherosclerotic disorders such as cardiac infarction, and stroke, asthma, psoriasis, chronic neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's, demyelinating diseases, AIDS immune deficiency, disorders of photoreceptor degeneration, and lens cataract formation, organ transplant rejection, cataracts, restenosis, muscular dystrophy, renal failure, cerebral vasospasm, pancreatitis, and diabetic nephropathy, among others, and diagnostic assays for such conditions.

  Excerpt(s): This invention relates to newly identified polynucleotides, polypeptides encoded by them and to the use of such polynucleotides and polypeptides, and to their production. More particularly, the polynucleotides and polypeptides of the present

invention relate to serine protease family, hereinafter referred to as HGBAB90. The invention also relates to inhibiting or activating the action of such polynucleotides and polypeptides. Proteases perform a variety of important functions in human physiology. Increasingly diseases are being identified where proteases are critical for the pathology of a particular disease. For these key proteases designing or screening for selective antagonists or agonists can lead to the development of new drugs. The serine proteases are a major family of proteases for which a large number are known. These have been reviewed by Rawlings & Barrett, (Methods Enzymol 244: 19-61, 1994). An example of the serine proteases is the mouse neuropsin (Chen et al. J Neurosci 15 (7 Pt 2): 5088-5097 1995). There remains a need for identification and characterization of further members of the serine protease family which can play a role in preventing, ameliorating or correcting dysfunctions or diseases, including, but not limited to, pulmonary **emphysema,** arthritis, multiple sclerosis, periodontal disease, cystic fibrosis, respiratory disease, thrombosis, cancer, cachexia, angina, glaucoma, inflamatory disorders, osteoporosis, cardiovascular disorders such as hypertension, atherosclerotic disorders such as cardiac infarction, and stroke, asthma, psoriasis, chronic neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's, demyelinating diseases, AIDS immune deficiency, disorders of photoreceptor degeneration, and lens cataract formation, organ transplant rejection, cataracts, restenosis, muscular dystrophy, renal failure, cerebral vasospasm, pancreatitis, and diabetic nephropathy.

Web site: http://www.delphion.com/details?pn=US06100059__

- **Diastereomeric pure trifluoromethyl ketone peptide derivatives as inhibitors of human leukocyte elastase**

  Inventor(s): Davies; Elwyn Peter (Macclesfield, GB), Pegg; Stephen John (Macclesfield, GB), Sependa; George Joseph (Macclesfield, GB), Veale; Chris Allan (Newark, DE)

  Assignee(s): Zeneca Limited (GB)

  Patent Number: 6,037,363

  Date filed: February 22, 1999

  Abstract: The present invention relates to pyrrolidine derivative compounds, and more particularly to the compound (S)-1-[(S)-2-(4-methoxybenzamido)-3-methylbutyryl]-N-[(S)-2-methyl-1-(trif luoroacetyl)propyl]pyrrolidine-2-carboxamide, shown by the formula I, a pharmaceutical composition comprising this compound in a crystalline form and a process for preparing the pharmaceutical composition. The compound of formula I is an inhibitor of human neutrophil elastase and is useful in the treatment of diseases in which the enzyme is implicated, such as, for example, **emphysema** and acute respiratory distress syndrome (ARDS).

  Excerpt(s): Because of HLE's apparent role, there has been considerable research effort in recent years towards the development of HLE inhibitors. In U.S. Pat. No. 4,910,190 is disclosed a series of structurally related peptidoyl trifluoromethane derivatives which are HLE inhibitors. We have now discovered that the specific, pyrrolidine derivative named above is a potent inhibitor of HLE, possessing a surprising advantage in that it is a single diastereoisomer having a crystalline form. This provides a basis for the present invention. To use an HLE inhibitor which cannot be isolated in a crystalline form as, or in the formulation of, a medicament for treating the disease conditions referred to above, poses significant problems, for example, in the manufacture of the compound or formulation to the purity levels and uniformity required for regulatory approval. It is therefore highly desirable to find a novel crystalline HLE inhibitor and even more

desirable to obtain a novel crystalline HLE inhibitor which is a single diastereoisomer. A further advantage of the compound of the invention is that it has been found to possess HLE inhibitory activity when administered orally. Prior to the present invention, the specific pyrrolidine derivative named above had not previously been prepared and therefore nothing was specifically known of its physical, chemical or pharmacological properties. According to the invention there is provided the compound (S)-1-[(S)-2-(4-methoxybenzamido)-3-methylbutyryl]-N-[(S)-2-methy-1-(trifl uoroacetyl)propyl]pyrrolidine-2-carboxamide, or a solvate thereof. Preferably the SSS diastereoisomer of formula I is in the anhydrous form, i.e. substantially or essentially free of the solvated (for example, hydrated) form. In this form, the SSS diastereoisomer has the advantageous property that it is non-hygroscopic. It also possesses the advantageous property that in the solid state it has good epimeric stability. Thus a particularly preferred form of the SSS diastereoisomer of formula I is a form containing less than 2% of the SSR diastereoisomer of formula I and being 95% or more in the anhydrous form.

Web site: http://www.delphion.com/details?pn=US06037363__

- **Elastase inhibitor and process for preparing the same**

  Inventor(s): Hong; Seok-Jin (Taejon, KR), Jung; Hyo-Il (Taejon, KR), Kang; Ke-Won (Taejon, KR), Kim; Dong-Ryoung (Seochun-Kun, KR), Lee; Ju-Yun (Taejon, KR)

  Assignee(s): Korea Advanced Institute of Science and Technology (Taejon, KR)

  Patent Number: 6,008,320

  Date filed: August 6, 1998

  Abstract: The present invention provides an elastase-inhibiting protein isolated ("Guamerin") from a Korean leech, Guameri (Hirudo nipponia) and a process for preparing the same. Guamerin is a protein of a molecular weight of 6,110 Da which is composed of 57 amino acid residues, whose active site is composed of 36-methionine and 37-isoleucine, which retains an inhibiting-activity highly specific to elastase, and which shows stability against heat as well as strong acids and alkalies. Guamerin of the present invention can be applied in the treatment of diseases associated with an excess level of elastase, such as rheumatoid arthritis, **emphysema,** and psoriasis.

  Excerpt(s): The present invention relates to a novel elastase inhibitor, more specifically, a novel protein isolated from a Korean leech, Guameri(Hirudo nipponia) which specifically inhibits elastase activity, and a process for preparing the same. Elastase is a serine protease capable of degrading mainly elastin and also connective tissue proteins such as collagen, cartilage, and fibronectin(see: Reilly, C. et al., Biochem. Biophys. Acta., 621: 147-167(1980); Mainardi, C. L. et al., J. Biol. Chem., 255: 5436-5441(1980)). Human leukocyte elastase is stored principally in neutrophils and the stored elastase is released, when neutrophils encounter foreign pathogens or antigens in blood, to degrade them so that body is protected from the harmful factors(see: Weisemann, G. et al., New Engl. J. Med., 303: 27-34(1980)). However, uncontrolled secretion of elastase which frequently results from aging of the cells or genetic defects may cause non-specific proteolysis and trigger destructive processes associated with various chronic diseases such as rheumatoid arthritis, **emphysema,** and psoriasis(see: Glinski, W. et al., J. Invest. Dermatol., 75: 481-487(1980); Snider, G. L., Med. Clin. North. Am., 65: 647-666(1981)): Rheumatoid arthritis is an inflammatory disease resulting from an excessive release of elastase which causes abnormal degradation of cartilage at joints of the knee and the finger in human; **emphysema** is also an inflammatory disease caused by the degradative

action of elastase excessively released from neutrophils which have come into the injured site of the lung tissue to prevent intrusion of pathogens from air; and, psoriasis is one of the representative skin diseases caused by elastase, which is characterized by distinct, reddish, slightly raised plaques-with adherent silvery scale.

Web site: http://www.delphion.com/details?pn=US06008320__

- **Episomal expression cassettes for gene therapy**

  Inventor(s): Chow; Yu-Hua (North York, CA), Hu; Jim (East York, CA), O'Brodovich; Hugh (Oakville, CA), Tsui; Lap-Chee (Etobicoke, CA)

  Assignee(s): HSC Research and Development Limited Partnership (Toronto, CA)

  Patent Number: 6,372,500

  Date filed: November 12, 1999

  Abstract: The invention consists of episomal expression cassettes for expression of a transgene in gene therapy. The expression cassettes consist of regulatory elements of the human cytokeratin gene and a transgene. The invention also includes of liposomes for transfection of epithelial tissue with the cassettes in treatment of cystic fibrosis, **emphysema,** cancers of epithelial origin arising in the lung or other organs.

  Excerpt(s): The invention relates to gene therapy episomal expression cassettes to express a transgene in epithelial cells. Demonstration of the feasibility of gene transfer to humans by a number of clinical trials stimulated considerable interest in gene therapy in the scientific community even though no therapeutic benefit has yet been offered to patients (7). Epithelial tissue, particularly lung epithelial tissue, has considerable potential as a target for gene therapy. The lung is a highly suitable organ for in vivo gene therapy treatment of patients with potentially lethal lung disorders, such as cystic fibrosis, cancers of epithelial origin and **emphysema** because of its large accessible epithelial and endothelial surface area (15). Both virus-based and non-virus-based methods can be used to deliver genes to lungs (6, 15). The use of liposomes as gene transfer agents seems to have some significant advantages for in vivo lung gene therapy (6, 15). First, liposomes offer a wide margin of safety with low toxicity and have already been used to deliver drugs to humans. They can be administered into the lungs as an aerosol, by direct lavage or following intravenous injection. A clinical trial in nasal epithelia showed no adverse effects; nasal biopsies showed no immuno-histological changes (4). Secondly, liposome-complexed DNA can be used to transfect both resting and dividing cells. In addition, large DNA constructs can be accommodated with liposomes for transfection. Finally and most importantly, liposome-mediated gene expression is episomal, thereby avoiding or reducing the risk of random chromosomal insertions. However, one of the major impediments to liposome-mediated in vivo gene therapy is that the currently available expression vectors only offer a very low level of transient transgene expression (15). Therefore, enhancement of the therapeutic gene expression would not only increase the efficacy, but also effectively decrease the already low levels of toxicity by reducing the dose of therapeutic reagent. The inefficient expression of transgenes in lung is, at least in part, due to the lack of proper lung-specific gene expression cassettes (15). An ideal expression cassette for human lung gene therapy should be safe and confer an appropriate level of tissue-specific expression for a reasonable duration. The rational design of expression cassettes for lung gene therapy relies on our knowledge of regulation of gene expression. Regulation of eukaryotic gene expression is a very complicated process.

Web site: http://www.delphion.com/details?pn=US06372500__

- **hNT-neuron human neuronal cells to replace ganglion cells**

  Inventor(s): Snable; Gary L. (Atherton, CA)

  Assignee(s): Layton Bioscience, Inc. (Sunnyvale, CA)

  Patent Number: 6,162,428

  Date filed: February 12, 1997

  Abstract: Disclosed herein is the treatment of vision loss in a mammal by transplanting an effective amount of hNT-Neuron cells. The treatment can be accomplished by injecting the cells into the retinal area of the eye. Additionally, the cells can be injected into the visual cortex of the brain. Conditions to be treated are vision loss due to optic nerve damage, including glaucoma, optic nerve sheath meningioma and glioma, Graves' ophthalmopathy, benign or malignant orbital tumors, metastatic lesions, tumors arising from the adjacent paranasal sinuses or middle cranial fossa, giant pituitary adenomas, brain tumors or abscesses, cerebral trauma or hemorrhage, meningitis, arachnoidal adhesions, pseudotumor cerebri, cavernous sinus thrombosis, dural sinus thrombosis, encephalitis, space-occupying brain lesions, severe hypertensive disease or pulmonary **emphysema.**

  Excerpt(s): The present invention is in the field of human transplantation and more particularly in the field of intraocular and intracranial transplantation of specially treated human cells which reestablish neuronal connections between the retina and the ocular cortex, which neurons having been damaged by glaucoma or other compression-causing injuries and diseases. Glaucoma is the occurrence of elevated intraocular pressure which causes progressive blindness in the form of gradual loss of peripheral fields of vision. It is an important cause of blindness and occurs in 1-2% of individuals over the age of 60. Often the disease is asymptomatic, as the patient painlessly and gradually loses vision. Before a diagnosis is made, the patient may have lost half of the one million optic nerve fibers in one eye. Today, intervention is focused on early detection, which depends on a routine eye examination which includes intraocular pressure measurement (tonometry), funduscropy with attention to the optic disc appearance, and visual field testing. In the normal eye, the optic cups are symmetric and the neural rim is pink. In glaucoma, either localized notching or generalized enlargement of the optic cup can be seen. The rim, although thinned, remains pink until late in the disease. The central optic cup diameter can be compared with the diameter of the disc. The ratio of the horizontal and vertical dimensions can be recorded. The normal cup-disc ratio is less than 0.2 to 0.3. Vertical disparity in one or both eyes is an early sign of glaucoma. Glaucoma is often asymmetric. The finding of asymmetry of the cup-disc ratio implies glaucoma. Early in the disease, visual field loss may include nonspecific constriction and small paracentral scotomas. Eventually, the arcuate nerve fiber bundle defects develop with a characteristic nasal step: The arcuate bundle defect extends to the nasal horizontal raphe to form a step-like configuration on kinetic visual field testing. The papillomacular bundle and vision are spared until late in the disease (HARRISON'S PRINCIPLES OF INTERNAL MEDICINE, 13.sup.th ed. Ed. By Isselbacher, Braunwald, Wilson, Martin, Fauci and Kasper. McGraw-Hill, New York City, 1996. Pp. 104-6). Intraocular pressure reflects the balance between the production and outflow of aqueous humor. The normal range for measurements by applanation tonometry (the tonometer applanates the corneal surface) is 2.09.+-.2.5 mmHg. Another method of measuring intraocular pressure is briefly indenting the cornea with a Schiotz tonometer.

Web site: http://www.delphion.com/details?pn=US06162428__

- **Method and apparatus for analyzing CT images to determine the presence of pulmonary tissue pathology**

  Inventor(s): Hoffman; Eric A. (Iowa City, IA), McLennan; Geoffrey (Iowa City, IA), Mitsa; Theophano (Waukesha, WI), Sonka; Milan (Iowa City, IA), Uppaluri; Renuka (Iowa City, IA)

  Assignee(s): The University of Iowa Research Foundation (Iowa City, IA)

  Patent Number: 6,466,687

  Date filed: February 11, 1998

  Abstract: A method and apparatus for analyzing CT images to determine the presence of pulmonary tissue pathology, such as in **emphysema,** IPF, sarcoid, etc. In accordance with one embodiment, a CT slice is selected to perform an automated, objective, and quantitative analysis of the slice. Initially, an image processing stage is performed, which includes segmentation and edgementation of the selected CT slice for preparation of a series of objective, quantitative measures to be performed on the slice. A region of interest (ROI) is selected on the CT slice in which these objective, quatitative measures are to be taken. The first set of objective, quantitative measures are first order texture measures that describe a frequency of occurrence of all gray levels assigned to pixels within the ROI of the image slice. The second set of objective, quantitative measures are second order texture measures that characterize the spatial interdependencies between particular pixels of the ROI. Fractal analysis could also be performed to provide additional objective, quantitative measures of the ROI. The ROI is classified to a particular tissue pathology class based upon an optimal subset of first or second order texture measures and fractal measures obtained. A color-coded output is displayed for visual presentation to a user indicating the different tissue pathology classes assigned to different regions of the CT slice.

  Excerpt(s): The present invention relates generally to the detection and diagnosis of tissue pathology using a diagnostic medical image, and, more particularly, to a method and apparatus for detecting and diagnosing the presence of pulmonary tissue pathology from CT images using an automated texture analysis procedure. Pulmonary **emphysema** is a common, debilitating, and progressive disorder of the lungs that may result from smoking. The disorder is caused by destruction of the alveolar walls of the lung parenchyma (i.e., lung tissue), which results in an abnormal enlargement of air spaces distal to the terminal bronchiole. Enlargement of these air spaces in the lungs impedes the exchange of oxygen in the air for carbon dioxide in the bloodstream. As a result of this impeded process, an individual experiences breathlessness, making ordinary tasks, once thought simple, labor intensive. While **emphysema** causes tissue in the lungs to atrophy, other pulmonary diseases, such as idiopathic pulmonary fibrosis (IPF) and sarcoidosis (sarcoid), cause the build-up of tissue in the lungs. Albeit the effects of **emphysema** and IPF and sarcoid might seem to be directly opposite from one another, IPF and sarcoid also suffer the same negative symptom of chronic fatigue. That is, IPF and sarcoid also impede the carriage of oxygen from the lungs to the bloodstream like **emphysema.**

  Web site: http://www.delphion.com/details?pn=US06466687__

- **Method and apparatus for pulmonary administration of dry powder.alpha.1-antitrypsin**

  Inventor(s): Eljamal; Mohammed (San Jose, CA), Patton; John S. (San Carlos, CA)

  Assignee(s): Inhale Therapeutic Systems (San Carlos, CA)

  Patent Number: 5,993,783

  Date filed: July 13, 1998

  Abstract: Dry powders of.alpha.1-antitrypsin are administered pulmonarily to patients to treat, for example, certain types of **emphysema.** The dry powder compositions may comprise aggregates of fine particles, which aggregates are friable and break-up upon dispersion in a flowing gas stream. Typically, the dispersed powders are captured in a chamber and subsequently inhaled by a patient for pulmonary treatment of **emphysema** and other conditions.

  Excerpt(s): Neutrophil elastase is a broad spectrum protease that is known to have access to the tissues of the lung. This protease is generally capable of degrading all major protein components of the alveolar interstitium. The unrestrained action of this protease, with its elastolytic properties can lead to the destruction of lung connective tissue and to the anatomic and functional derangements of pulmonary **emphysema.** Smith, et al., J. Clin. Invest. 84:1145-1154 (1989).alpha.1-antitrypsin (".alpha.1AT") is a protease inhibitor with inhibitory activity toward neutrophil elastase. A deficiency of.alpha.1-antitrypsin in the lower respiratory tract has been found to be central to the pathogenesis of **emphysema** due to the critical role of.alpha.1AT in protecting alveolar structures from neutrophil elastase.alpha.1AT deficiency is a genetic disorder characterized by low plasma and lung levels of the inhibitor and the development of **emphysema** by the third to fourth decades. In addition to genetic deficiencies in.alpha.1AT, it has been found that the lungs of cigarette smokers are burdened with neutrophils. In particular, significantly increased numbers of neutrophils have been found in cell suspensions isolated from bronchoalveolar lavage fluid and from open lung biopsies of both normal and sarcoid cigarette smokers compared with non-smokers. Hunnighake and Crystal, Am. Rev. Respir. Dis. 128:833-838 (1983).

  Web site: http://www.delphion.com/details?pn=US05993783__

- **Method for predicting risk of developing chronic pulmonary emphysema**

  Inventor(s): Nakayama; Katsutoshi (Sendai, JP), Okinaga; Shoji (Boston, MA), Sasaki; Hidetada (Sendai, JP), Yamaya; Mutsuo (Sendai, JP)

  Assignee(s): President of Tohoku University (Sendai, JP)

  Patent Number: 6,436,645

  Date filed: November 22, 2000

  Abstract: An objective of this invention is to provide a method for predicting the risk of subject developing chronic pulmonary **emphysema.** To achieve the objective, this invention provides a method for predicting the risk of subject developing chronic pulmonary **emphysema** comprising determining the number of GT repeats within a GT repeat sequence located upstream of hemeoxygenase-1, in which if the number of the GT repeats is not less than 30, the subject has a high risk of developing chronic pulmonary **emphysema.**

Excerpt(s): This application is based upon and claims the benefit of priority from the prior Japanese Patent Application No. 11-334248, filed Nov. 25, 1999, the entire contents of which are incorporated herein by reference. The present invention relates to a method for predicting the risk of developing chronic pulmonary **emphysema.** Chronic pulmonary **emphysema** (hereinafter referred to as "CPE") has increased due to the changing circumstances in the Japanese society, habitual smoking, and aging. When a person suffers from chronic dyspnea, a daily life is limited. Furthermore, respiratory tract infection leads to breathing difficulties (respiratory insufficiency). Therefore, it is an urgent business to clarify pathogenesis and prophylaxis of CPE.

Web site: http://www.delphion.com/details?pn=US06436645__

- **Method for the prevention of tissue elastic fiber injury**

Inventor(s): Cantor; Jerome O. (Bronx, NY)

Assignee(s): The Trustees of Columbia University in the City of New York (New York, NY)

Patent Number: 6,391,861

Date filed: May 14, 1998

Abstract: The subject invention is directed to the prevention of elastic fiber injury by administering HA or any other polysaccharide or carbohydrate moiety that binds to and coats elastic fibers, thereby preventing enzymes, oxidants, or other injurious agents from contacting and damaging these fibers. The method may be used to prevent elastic fiber damage which occurs to the skin and blood vessels as a consequence of aging, to the uterus during pregnancy, and in diseases such as pulmonary **emphysema,** aortic aneurysm, and joint disease. The treatment is intended for humans and a variety of other mammals. The polysaccharide or carbohydrate moiety may be administered orally, cutaneously, subcutaneously, intravenously, intratracheally, or by any other route deemed efficacious. It may be administered alone or in combination with another polysaccharide or carbohydrate moiety, with or without a carrier such as saline solution, DMSO, alcohol or water. It may be naturally occurring, chemically modified, or artificially synthesized. The effective daily amount of the polysaccharide or carbohydrate moiety is from about 0.1.mu.g/kg to about 1 mg/kg of body weight.

Excerpt(s): Throughout this application, various publications are referenced by numbers. The full citations are listed at the end of the specification immediately preceding the claims. Elastic fibers are a prominent component of the extracellular matrix and play an important role in determining the mechanical properties of tissues. By virtue of their distensibility, elastic fibers permit tissues to function normally despite the application of external forces. In the lung, for example, interstitial and pleural elastic fibers facilitate tissue recoil following inspiration, preventing permanent distention of the organ and maintaining the flow of gases within airways. Damage to these fibers causes dilatation and rupture of alveoli, resulting in pulmonary **emphysema** (1,2). Despite the importance of maintaining the integrity of elastic fibers, there is currently no effective means of protecting them from damage. Since these fibers are susceptible to degradation by enzymes known as elastases, various elastase inhibitors have been tested as a possible means of preventing elastic fiber injury (1,3). In particular, a naturally occurring inhibitor, alpha-1-antiproteinase, has recently been given to individuals who normally lack this inhibitor in an attempt to slow the progression of elastic fiber breakdown which leads to pulmonary **emphysema** (4). Such a treatment strategy assumes, however, that elastic fiber injury is caused by a specific type of biochemical

derangement, i.e. alpha-1-antiproteinase deficiency. If damage to these fibers represents a more general reaction to a variety of insults (with elastases playing a variable role), then enzyme inhibition may have only limited efficacy.

Web site: http://www.delphion.com/details?pn=US06391861__

- **Method for the treatment of alpha-1-antitrypsin deficiency and related pathologies**

  Inventor(s): Burrows; Jon A. J. (WU School of Medicine, 4905 Children's Pl., Room 5309, St. Louis, MO 63110), Perlmutter; David H. (Children's Hospital of Pittsburgh, 3705 Fifth Ave., Pittsburgh, PA 15213), Teckman; Jeffery H. (WU School of Medicine, 4905 Children's Pl., Room 5309, St. Louis, MO 63110), Willis; Lauren K. (Center for Pediatric Research, 855 W. Brambleton Ave., Norfolk, VA 23510-1001)

  Assignee(s): none reported

  Patent Number: 6,403,646

  Date filed: June 30, 2000

  Abstract: A method for the treatment of alpha-1-antitrypsin deficiency caused by the protease inhibitor type Z mutation by administration of phenylbutyric acid derivatives. Also disclosed are methods for the prevention and treatment of liver injury and **emphysema** associated with alpha-1-antitrypsin deficiency by administration of phenylbutyric acid derivatives.

  Excerpt(s): This invention relates to methods for the use of phenylbutyric acid and its pharmaceutically acceptable derivatives to treat alpha-1-antitrypsin deficiency in vertebrate animals. More particularly this invention relates to the treatment and prevention of pathologies resulting in alpha-1-antitrypsin deficiency including liver disease and **emphysema.** More particularly, this invention relates to the use to phenylbutyric acid and its pharmaceutically acceptable derivatives to increase secretion by the liver of alpha-1-antitrypsin in animals with alpha-1-antitrypsin deficiency caused by the protease inhibitor type Z (PiZ) mutation. Alpha-1-antitrypsin deficiency is a relatively common genetic disorder that predisposes affected individuals to liver disease and/or pulmonary **emphysema.** The most common type of alpha-1-antitrypsin deficiency termed protease inhibitor type Z (PiZ), is transmitted as an autosomal recessive trait and affects approximately 1 in 1700 live births in most Northern European and North American populations. The PiZ mutation is a single nucleotide substitution that results in a single amino acid substitution (glutamate 342 to lysine). The replacement of glutamate 342 with a lysine apparently prevents normal folding of the protein. Although not all individuals with the PiZ mutation develop clinical symptoms, it is the most common genetic cause of acute and chronic liver disease in children and the most common genetic diagnosis in children undergoing liver transplantation. The incidence of **emphysema** or destructive lung injury in this population is not known, but cigarette smoking markedly increases the likelihood of lung injury and accelerates the course of the disease in PiZ individuals. The major physiological function of alpha-1-antitrypsin is the inhibition of neutrophil elastase, cathepsin G and proteinase 3. The alpha-1-antitrypsin produced in individuals with PiZ alpha-1-antitrypsin deficiency is functionally active, although there may be a decrease in its specific elastase inhibitory capacity. The predominant site of alpha-1-antitrypsin synthesis is the liver, however, it is also synthesized in extrahepatic cell types including macrophages, intestinal epithelial cells and intestinal Paneth cells. In human hepatoma cells alpha-1-antitrypsin is synthesized as a 52 kD precursor that undergoes post translational dolichol phosphate-linked glycosylation at three asparagine residues, and also undergoes tyrosine sulfation.

The protein is secreted as a 55 kD native single-chain glycoprotein with a half-time for secretion of 35 to 40 minutes. The half-life in plasma of type M alpha-1-antitrypsin (.alpha.1-AT) (PiM is the normal allotype) is approximately five days. The half-life of the PiZ mutant protein (.alpha.1-ATZ) is slightly less, but this difference is insufficient to account for the low plasma levels of alpha-1-antitrypsin in homozygous PiZ individuals.

Web site: http://www.delphion.com/details?pn=US06403646__

- **Methods for treating respiratory disease**

  Inventor(s): McMichael; John (Delanson, NY)

  Assignee(s): Milkhaus Laboratory, Inc. (Delanson, NY)

  Patent Number: 5,955,442

  Date filed: February 13, 1998

  Abstract: Methods for treating respiratory disease, including cystic fibrosis, **emphysema,** bronchitis, and sinusitis are presented. Methods comprise administering to a patient an effective amount of DNA in a manner so as not to be effect gene transfer and expression.

  Excerpt(s): The present invention relates to methods for treatment of pulmonary disorders. The present invention provides methods for treatment of pulmonary diseases. Such diseases, including cystic fibrosis, **emphysema,** chronic bronchitis, sinusitis, and the common cold, have in common bronchial or sinus congestion, production of large amounts of sputum, and the possibility of secondary bacterial infection requiring antibiotic therapy. The most serious of those diseases is cystic fibrosis, a genetic disorder of exocrine function characterized by abnormally viscous mucus secretions leading to chronic pulmonary obstruction, pancreatic insufficiency and elevated sweat sodium and chloride levels. Cystic fibrosis is often fatal. The viscosity of sputum produced by cystic fibrosis patients is thought to be due to its high content of DNA. Diseases such as bronchitis, **emphysema,** sinusitis, and the common cold are generally less severe than cystic fibrosis, but those diseases also may result in production of large amounts of sputum. As with cystic fibrosis, other pulmonary diseases frequently lead to secondary bacterial infections. Treatment of pulmonary diseases generally requires antibiotic therapy which is frequently ineffective. Recently, however, cystic fibrosis has been treated using DNase. The rationale for such therapy is that degrading DNA in sputum reduces the viscosity of the sputum and results in an increased ability of the patient to evacuate sputum from the lungs and nasal passages. However, no known report advocates using DNA itself as a treatment for any pulmonary infection.

  Web site: http://www.delphion.com/details?pn=US05955442__

- **Methods for treatment of Emphysema using 13-cis retinoic acid**

  Inventor(s): Belloni; Paula N (Half Moon Bay, CA)

  Assignee(s): Syntex (U.S.A.) LLC (Palo Alto, CA)

  Patent Number: 6,339,107

  Date filed: August 2, 2000

  Abstract: The current invention is directed to methods of treating or preventing **emphysema,** pharmaceutical compositions suitable for the treatment or prevention of

emphysema and methods for delivering formulations into the lung of a mammal suffering from **emphysema.**More generally, the invention encompasses the use of 13-cis-retinoic acid to treat or prevent certain chronic obstructive airway disorders, particularly chronic obstructive pulmonary disease including chronic bronchitis, **emphysema** and asthma in mammals, especially humans that smoke or smoked cigarettes. In another aspect, the present invention encompasses the use of pharmaceutical compositions of 13-cis-retinoic acid to treat **emphysema.** Moreover, the current invention encompasses the use of electrohydrodynamic aerosol devices, aerosol devices and nebulizers to deliver formulations of 13-cis-retinoic acid into the lung of a mammal suffering from **emphysema.** The invention also encompasses the systemic use as well as the local use of 13-cis-retinoic acid. In a another aspect the current invention encompasses a pharmaceutical composition for preventing **emphysema** in a human at risk of **emphysema** through administration of a amount of 13-cis-retinoic acid, or a pharmaceutically acceptable salt, hydrate, solvate, or pro-drug thereof in a pharmaceutically acceptable carrier, that is sufficient to prevent **emphysema.**

Excerpt(s): The invention relates to methods of treating **emphysema** with 13-cis-retinoic acid, pharmaceutical compositions of 13-cis-retinoic acid useful in the treatment of **emphysema** and methods for delivering formulations of 13-cis-retinoic acid to the lung of a mammal suffering from **emphysema.** 13-cis-retinoic acid is also known as isotretinoin, AGN 190013, Neovitamin A acid, Ro-4-3780, 13-cis-.beta.-Retinoic acid and 13-cis-Vitamin A acid. 13-cis-retinoic acid is sold under the tradenames Accutane.RTM., Roaccutan.RTM. and Roaccutane.RTM. for the treatment of severe recalcitrant nodular acne (Physicians'Desk Reference 54.sup.th Ed., p. 2610, 2000; Peck et al., N. Eng. J Med.; Peck et al., U.S. Pat. No. 5,698,593). 13-cis-Retinoic acid has also been reported to be effective in treating psychotic illnesses such as schizophrenia (Straw, U.S. Pat. No. 4,808,630) and cancer of head, neck and lung (Tomas et al., Annals of Oncology, 1999, 10, 95; Benner et al., Seminars in Hematology, 1994, 31, 26). 13-cis -Retinoic acid is currently in clinical trials for treatment of these forms of cancer at a number of locations (e.g., University of Texas SW Medical Center, Dallas Tex.; University of Texas MD Anderson Cancer Center, Houston, Tex.; Department of Veteran Affairs Medical Center, Temple, Tex.). 13-cis-retinoic acid is a member of the retinoid class of compounds which are structural analogues of vitamin A and include both natural and synthetic compounds. Naturally occurring retinoid compounds such as all trans retinoic acid ("ATRA"), 9-cis -retinoic acid, trans 3-4 didehydroretinoic acid, 4-oxo retinoic acid and retinol are pleiotrophic regulatory compounds that influence a large number of inflammatory, immune and structural cells.

Web site: http://www.delphion.com/details?pn=US06339107__

- **Orally-active elastase inhibitors**

  Inventor(s): Angelastro; Michael R. (Mason, OH), Burkhart; Joseph P. (West Chester, OH), Peet; Norton P. (Cincinnati, OH)

  Assignee(s): Merrell Pharmaceuticals, Inc. (Bridgewater, NJ)

  Patent Number: 6,265,381

  Date filed: January 28, 2000

  Abstract: This invention relates to novel morpholinourea and related derivatives of pentafluoroethyl peptides which are orally active elastase inhibitors. These compounds are useful in the treatment of various inflammatory diseases and **emphysema.**

Excerpt(s): This invention relates to orally-active elastase inhibitors useful for a variety of physiological end-use applications. In its broad aspects, this invention relates to analogs of peptidase substrates in which the carboxy terminal carboxyl group has been replaced by a pentafluoroethylcarbonyl (--C(O)C.sub.2 F.sub.5)group and in which the amino terminal amino acid is protected by various heterocycle-containing groups such as a 4-morpholinecarbonyl group. These elastase inhibitors exert valuable pharmacological activities and therefore have useful physiological consequences in a variety of disease states. In its more specific aspects, this invention relates to pentafluoroethylcarbonyl analogs of certain elastase substrates which have various heterocyclic containing protecting groups which are useful in inhibiting elastase, the inhibition of which will have useful physiological consequences in a variety of disease states.

Web site: http://www.delphion.com/details?pn=US06265381__

- **Oxygen enriched air supply apparatus**

  Inventor(s): Himelreich; Louis (Wilmington, DE), Nemser; Stuart Marshall (Wilmington, DE)

  Assignee(s): Compact Membrane Systems, Inc. (Wilmington, DE)

  Patent Number: 6,126,721

  Date filed: November 16, 1998

  Abstract: A portable breathing air supply apparatus uses a membrane separation module to obtain oxygen enriched air from ambient air which is blown into the module by an electrically powered fan. Oxygen enriched air is withdrawn from the permeate side of the membrane by a vacuum pump and is stored in a reservoir while the user exhales. In a preferred mode, a conserver valve in a tube leading from the reservoir to the user's mouth or nose is triggered to feed the enriched air for a preselected duration after a sensor in the tube detects onset of inhalation. Power for the electrical components can be supplied by batteries. The portable apparatus is sufficiently compact and light to be transported by persons weakened by certain chronic breathing disorders, such as chronic obstructive pulmonary disease and **emphysema,** and thus frees the user to roam for long periods away from a primary source of oxygen.

  Excerpt(s): This invention relates to an apparatus for generating oxygen enriched air. More specifically, it relates to a light weight, compact, portable apparatus using selectively permeable hollow fiber membranes to produce breathable, oxygen enriched air from ambient air. The inhalation of oxygen enriched air is sometimes prescribed for treatment of certain chronic breathing disorders, such as chronic obstructive pulmonary disease and **emphysema.** The traditional methods for generating oxygen enriched air for such treatment generally utilize stationary equipment to manufacture oxygen chemically, e.g. by electrolysis or pressure swing adsorption, or to refine oxygen from air cryogenically. Stationary sources of oxygen enriched air are unsuitable for many patients because the roaming range of the user is limited to the immediate vicinity of the enriched air supply. Oxygen produced by a stationary source can be stored in tanks and carried by the patient to be consumed away from the source. However, oxygen is usually stored under pressure to maximize storage capacity. Storage tanks capable of holding compressed gas are normally bulky and heavy. Patients who suffer from breathing difficulty are likely to be weak and generally are not able to easily handle heavy compressed oxygen tanks. Furthermore, tank capacity normally limits usage to at most about a couple of hours away from the primary source of oxygen enriched air.

Web site: http://www.delphion.com/details?pn=US06126721__

- **Polynucleotide encoding human serpin**

  Inventor(s): Holloway; James L. (Seattle, WA)

  Assignee(s): ZymoGenetics, Inc. (Seattle, WA)

  Patent Number: 6,524,822

  Date filed: November 20, 2000

  Abstract: Members of the serine protease family play a role in carefully controlled processes, such as blood coagulation, fibrinolysis, complement activation, fertilization, and hormone production. The enzymatic activity of the serine proteases is regulated in part by serpins, serine protease inhibitors. Serpin dysfunction is associated with various disorders, including **emphysema,** blood clotting disorders, cirrhosis, Alzheimer disease, and Parkinson disease. Zserp11 is a new member of the serine protease inhibitor family.

  Excerpt(s): The present invention relates generally to a new gene that encodes an enzyme inhibitor. In particular, the present invention relates to a novel serpin, designated "Zserp11," and to nucleic acid molecules encoding Zserp11. Endogenous proteolytic enzymes provide a variety of useful functions, including the degradation of invading organisms, antigen-antibody complexes, and certain tissue proteins that are no longer necessary. The serine proteases comprise a large family of enzymes that use an activated serine residue in the substrate-binding site to catalytically hydrolyze peptide bonds. Typically, this serine residue can be identified by the irreversible reaction of its side chain hydroxyl group with diisopropylfluorophosphate. Serine proteases participate in carefully controlled processes, such as blood coagulation, fibrinolysis, complement activation, fertilization, and hormone production. Normally, serine proteases catalyze limited proteolysis, in that only one or two specific peptide bonds of the protein substrate are cleaved. Under denaturing conditions, serine proteases can hydrolyze multiple peptide bonds, resulting in the digestion of peptides, proteins, and even autolysis. Several diseases are thought to result from the lack of regulation of serine protease activity, including **emphysema,** arthritis, cancer metastasis, and thrombosis.

  Web site: http://www.delphion.com/details?pn=US06524822__

- **Protein having proteinase inhibitor activity**

  Inventor(s): Davies; Christopher (Walnut Creek, CA), Delaria; Kathy (Walnut Creek, CA), Roczniak; Steve (Lafayette, CA)

  Assignee(s): Bayer Corporation (Berkeley, CA)

  Patent Number: 6,294,648

  Date filed: July 20, 1999

  Abstract: BTL.009 is a novel human serine proteinase inhibitor of the Kunitz family that exhibits greater potency towards neutral serine proteinases, particularly leukocyte elastase, and chymotrypsin than towards trypsin-like proteinases. BTL.009, or variants thereof, may be employed as therapeutics in diseases such as **emphysema,** idiopathic pulmonary fibrosis, adult respiratory distress syndrome, cystic fibrosis, rheumatoid

arthritis, organ failure, and glomerulonephritis in which uncontrolled proteolysis due to neutral serine proteinase activity results in tissue damage.

Excerpt(s): This invention relates to newly identified polynucleotides, polypeptides encoded by such polynucleotides, the use of such polynucleotides and polypeptides, as well as the production of such polynucleotides and polypeptides. More particularly, the polypeptide of the present invention has been identified as a member of the Kunitz serine proteinase inhibitor family and is hereinafter referred to as BTL.009. The inflammatory response after surgeries, trauma and infection involves neutrophil activation and infiltration into the injured tissue. The activated neutrophils release the neutral serine proteinases leukocyte elastase, cathepsin G and proteinase 3, which, if not properly controlled, cause abnormal connective tissue turnover and result in severe damage to healthy tissue (1-3, 81). The uncontrolled proteolysis can lead to a myriad of diseases including **emphysema,** idiopathic pulmonary fibrosis, adult respiratory distress syndrome, cystic fibrosis, rheumatoid arthritis, organ failure, and glomerulonephritis. Proteins capable of inhibiting the neutral serine proteinases released by neutrophils can have therapeutic efficacy in treating inflammatory diseases. In patients suffering from hyperdynamic septic shock, plasma levels of the serine proteinase inhibitors antithrombin III, alpha 2-macroglobulin and inter-alpha-trypsin inhibitor, as well as those of various clotting, complement and other plasma factors, are significantly decreased (5). In an experimental endotoxemia model, the reduction in the plasma levels of these factors was considerably diminished by the intravenous injection of a soybean-derived leukocyte elastase and cathepsin G inhibitor, indicating that these neutral proteinases are at least partially responsible for the proteolysis of the plasma factors. In addition, the survival rate in the rat lethal peritonitis model (cecal ligation and puncture-induced septic shock model) was improved by treatment with the second domain of human urinary trypsin inhibitor (2), which has been shown to inhibit leukocyte elastase and cathepsin G (6, 7).

Web site: http://www.delphion.com/details?pn=US06294648__

- **Respiratory timing and lung deflation method and device**

  Inventor(s): Hillsman; Deane (870 El Chorro Way, Sacramento, CA 95864-5244)

  Assignee(s): none reported

  Patent Number: 6,626,843

  Date filed: September 28, 2001

  Abstract: A portable respiratory prompting device using simple visual and/or auditory means to indicate the onset of inspiration and expiration to prompt a subject into more desirable breathing patterns. Inspiration and expiration are indicated by LED's and simple high and low pitched "beep" sounds. The device is particularly suited for activating previously learned breathing patterns from visual biofeedback training. Optionally patients with **Emphysema** or Asthma may activate an button producing a prolonged expiratory phase to further lung deflation. It is also suited to prompt patients with Hyperventilation Syndrome attacks to slower breathing, and breathing control of subjects in stressful environments such as aircraft pilots or underwater divers, wherein an optional waterproof model is available. It may control breathing in a variety of applications such as pregnant subjects doing Lamaze breathing exercises and athletes in training. It may also be incorporated into clock mechanisms for day and night prompting.

Excerpt(s): This invention relates to improved methods and apparatus to prompt patients with lung disease, and other subjects, into more physiologically appropriate breathing patterns by simple visual and auditory biofeedback means. Hilisman incorporates by reference his U.S. Pat. No. 3,991,304 which describes a sophisticated and complex visual biofeedback device suitable only for medical professional use. This present invention extends that concept into a simple portable device suitable for use under field operational conditions, with both visual and auditory biofeedback means suitable for individual subject use in a lower technical environment. A wide variety of timing metronomes of both mechanical and electrical design have been well known in the music industry for many years. Almost all have been simple devices designed to give an auditory signal of equal periodicity and permitting only an overall rate adjustment. More modern electronic music metronome devices permit a wide spectrum of timing signals suitable for music timing and rhythm coordination needs, and some with visual prompting. This present invention relates to a timing device unique for medical needs wherein the overall rate and the relative timing of inspiration and expiration are adjustable, in essence therefore an "asynchronous metronome" specific to medical respiratory needs. In the course of using Hillsman's advanced visual biofeedback training device, U.S. Pat. No. 3,991,304 it was discovered that native breathing patterns in diseased **emphysema** patients could be altered and that these altered breathing patterns were retained in part (Reference: A Biofeedback Method To Alter Breathing Patterns In COPD; Hilisman, D. and Lillington, G. A.; Third International Conference on Pulmonary Rehabilitation and Mechanical Ventilation; Mar. 12, 1991--Reference: A Visual Biofeedback Method To Define And Teach Breathing Patterns, and, Clinical Experience With A Visual Biofeedback Method In COPD Rehabilitation; Hillsman, D.; International Society for the Advancement of Respiratory Psychophysiology; Second Annual Meeting, Oct. 9, 1995, Biological Psychology, Vol. 43, Issue 3, Jun. 28, 1996, pages 261 and 243-244. In some unknown manner it is apparent these learned breathing patterns are being imprinted in the patient's subconscious, and recalled and used with a variable degree of accuracy. Though it is usually easy to get patients to follow breathing pattern analogs using the sophisticated visual device, the problem of proper breathing patterns in the home environment remained. Furthermore, many patients would revert to their previous inefficient native breathing patterns under conditions of stress or with the passage of time. It was discovered with the patient blinded, a simple auditory signal to breathe in and out at the appropriate points in the breathing cycle was highly effective in prompting patients into an accurate reproduction of the breathing waveform analog. Thus the concept of the instant invention was created, to activate these learned breathing patterns in a more reliable and accurate manner by means of an auditory "beep" (high pitched) and the beginning of inspiration and another "beep" (low pitched) at the beginning of expiration. Further, it was considered desirable to use the familiar and soothing "tick/tock" sound of a grandfather clock as the auditory prompt as the preferred embodiment, though the concept could also be implemented with a variety of brief or continuous individual sounds or musical sounds or breath sounds of inspiration and expiration.

Web site: http://www.delphion.com/details?pn=US06626843__

- **Surgical appliance for the treatment of pulmonary emphysema**

  Inventor(s): Rebuffat; Carlo (Via Canova, 27-Milan, IT)

  Assignee(s): none reported

  Patent Number: 6,123,663

  Date filed: December 23, 1998

  Abstract: Surgical appliance for the treatment of pulmonary **emphysema** consisting of a sheath (1) made up of a biocompatible elastic material provided with a hole (4) suitable for the passage of the bronchia and vessels of the lung onto which the sheath (1) is to be applied. Once applied onto the lungs of an emphysematous, the surgical appliance according to the present invention remarkably improves his breathing functionality without resorting to traumatic surgical operations, such as for instance the partial removal or the plication of the pulmonary parenchyma.

  Excerpt(s): The present invention relates to a surgical appliance for the treatment of pulmonary **emphysema,** and in particular to a surgical appliance which, once applied onto the lungs of an emphysematous, remarkably improves his breathing functionality without resorting to traumatic surgical operations, such as for instance the partial removal or the plication of the pulmonary parenchyma. It is acknowledged that pulmonary **emphysema** has always been considered a disease that mainly, if not exclusively, relates to internal medicine and pneumology. The medical therapy of pulmonary **emphysema,** based upon breathing rehabilitation and use of specific medicines, is effective both as a therapeutic approach and in the preparation for a possible surgical operation. Surgery of pulmonary **emphysema,** preferably based upon bullectomy and pulmonary transplant, has had so far an absolutely secondary role in the therapy of this disease. Recently Cooper has instead proposed, with great success, a surgical operation that revolutionizes the treatment of pulmonary **emphysema** thereby resuming a procedure developed by Brantigan in 1959 and forgotten for many years. This operation, known as lung volume reduction, consists of a reduction of the volume occupied by the emphysematous lung through surgically removing 20 to 25% of the total mass of parenchyma, in particular its functionally hypoactive peripheral areas. While the lung volume reduction seems to be illogical for the treatment of patients affected by breathing insufficiency, this kind of operation is based upon precise physiopathological fundamentals which justify the execution and the good clinical results. Indeed, the lung with a reduced volume exerts a higher elastic retraction force against the thoracic cage, thereby improving both the volumetric balance of the lung/thoracic cage system and the efficiency of the inspiratory muscles. Such an improvement is due to the fact that the emphysematous lung, less elastic than a healthy lung, tends to expand more than the usual, especially in the apical areas, causing the expansion of the thoracic cage, which is no longer subject to the elastic retraction force of the lung.

  Web site: http://www.delphion.com/details?pn=US06123663__

- **Treatment of emphysema using RARy selective retinoid agonists**

  Inventor(s): Belloni; Paula Nanette (Half Moon Bay, CA), Klaus; Michael (Weil am Rhein, DE)

  Assignee(s): Syntex (U.S.A.) LLC (Palo Alto, CA)

  Patent Number: 6,300,350

  Date filed: October 18, 2000

  Abstract: This invention provides methods of treating **emphysema** and other diseases associated with alveolar damage by treatment with an RAR.gamma. selective agonist. In another aspect, this invention provides methods of promoting tropoelastin gene expression and alveolar matrix repair by contacting the pulmonary intestitial fibroblast with an RAR agonist, preferably an RAR.gamma. selective agonist.

  Excerpt(s): This invention relates to methods of treating **emphysema** to regenerate functional alveoli using retinoic acid receptor agonists, in particular a retinoic acid receptor agonist that is RAR.gamma. selective. Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality, ranking third and fourth as the leading cause of death in the European Union and North America respectively. COPD is characterized by reduced maximum expiratory flow that does not change over several months and persists for 2 or more consecutive years. Patients with the most severe form of COPD generally present with a significant degree of **emphysema.** Emphysema is defined anatomically by permanent airspace enlargement distal to the terminal bronchioles, and it is characterized by gradual loss of lung recoil, alveolar destruction, decreased alveolar surface area and gas exchange, leading to a reduced FEV1 (American Thoracic Society: Am. J. Resp. and Critical Care 152: S77-S124, 1995). Impaired gas exchange and reduction in expiratory flow are characteristic physiological abnormalities from which **emphysema** patients suffer. The main symptom of severely affected **emphysema** patients is shortness of breath during minimal physical activity.

  Web site: http://www.delphion.com/details?pn=US06300350__

- **Treatment of emphysema with retinoic acid or other retinoids by inducing formation of gas-exchange units (alveoli)**

  Inventor(s): Massaro; Donald (Washington, DC), Massaro; Gloria (Washington, DC)

  Assignee(s): Georgetown University School of Medicine (Washington, DC)

  Patent Number: 5,998,486

  Date filed: July 7, 1998

  Abstract: This invention relates to the use of retinoic acid, its esters and analogues thereof, for treatment of **emphysema.** The method comprises administration of a composition containing an effective amount of a retinoic acid, or an ester or an analoge thereof, to induce alveolar formation.

  Excerpt(s): This invention relates to the treatment of **emphysema** using retinoic acid, their esters and analogues thereof. Pulmonary **emphysema** is a common disease in which destruction of the lung's gas-exchange structures (alveoli) leads to inadequate oxygenation, disability and, frequently, death. Lung transplantation has previously provided the only means of remediation. Alveoli are formed by the developmentally regulated subdivision of saccules that constitute the gas-exchange region of the immature lung. The molecular signals responsible for the formation of septa and for

their spacing are poorly understood. However, in the rat retinoids may play a key regulatory role. Fibroblasts rich in vitamin A (retinol) storage granules occupy a large fraction of the alveolar wall when septa are being formed. During the same period, the concentration of cellular-retinol binding protein I, cellular retinoic acid-binding Protein I, and nuclear retinoic acid receptor-.tau. mRNA peak in the lung. Treatment with dexamethasone, a glucocorticosteroid hormone, prevents septation in a seemingly irrevocable fashion, and diminishes the expression in the lung of cellular retinol-binding protein and retinoic acid receptor-.beta. mRNA.

Web site: http://www.delphion.com/details?pn=US05998486__

- **Use of metalloproteinase inhibitors in the treatment and prevention of pulmonary emphysema**

  Inventor(s): Chada; Kiran (North Brunswick, NJ), D'Armiento; Jeanine (New York, NY)

  Assignee(s): The Trustees of Columbia University in the City of New York (New York, NY)

  Patent Number: 6,608,112

  Date filed: October 10, 2000

  Abstract: The invention provides a use of a metalloproteinase inhibitor for the preparation of a pharmaceutical composition for treating human pulmonary **emphysema** which comprises admixing the metalloproteinase inhibitor in an amount effective to treat human pulmonary **emphysema** and a pharmaceutically acceptable carrier. This invention also provides a pharmaceutical composition which comprises a metalloproteinase inhibitor in an amount effective to treat human pulmonary **emphysema** and a pharmaceutically acceptable carrier.

  Excerpt(s): Pulmonary **emphysema,** the major component leading to morbidity and mortality in chronic obstructive pulmonary disease (COPD), is the fourth leading cause of death in the United States. Approximately 15 million Americans are affected by COPD with an increasing incidence in women. Smoking is the major risk factor for COPD and accounts for over 90% of cases seen worldwide. Despite this finding, the standard treatment for COPD has changed little over the past 20-30 years. The etiology of **emphysema** is multiplex with a variety of different injuries leading to the disease, including structural damage to the lung, defective proteinase inhibitors and diseases which result in overproduction of neutrophils within the lung (Aaron, 1983). Currently the major hypothesis for the pathogenesis of **emphysema** is the protease-antiprotease theory (Janoff, 1985). This states that an imbalance between the levels of degradative enzymes and their respective inhibitors damages the connective tissue matrix components of the lung. Emphysema is estimated to affect 1.6 million Americans and has been shown to be directly related to cigarette smoking. Although the primary mechanism leading to lung destruction in this disease is believed to be secondary to an imbalance between proteases and antiproteases, direct evidence of an increase in destructive enzymes within the lung parenchyma has never been demonstrated. The hypothesis was based mainly on the induction of **emphysema** in animals through intratracheal instillation of nonspecific proteolytic enzymes (Gross et al., 1965). However, the major-focus of many studies has concentrated on elastase as the primary destructive protease due to two particular observations. First, the association between the absence of alpha-1 antitrypsin (an inhibitor of elastase) and **emphysema** was made through the characterization of the rare hereditary disease, alpha-1 antitrypsin deficiency (Laurell and Erikson, 1963). Secondly, pancreatic and leukocyte elastase

produce an emphysema-like phenotype experimentally when instilled intratracheally into certain animal species (Janoff et al., 1977). By contrast, when bacterial collagenase was injected into the lungs of hamsters, no emphysematous lesions developed (Johansen and Pierce, 1972).

Web site: http://www.delphion.com/details?pn=US06608112__

- **Val-pro containing.alpha.-keto oxadiazoles as serine protease inhibitors**

  Inventor(s): Gyorkos; Albert C. (Westminster, CO), Spruce; Lyle W. (Chula Vista, CA)

  Assignee(s): Cortech Inc. (Bedminster, NJ)

  Patent Number: 6,001,813

  Date filed: June 3, 1998

  Abstract: The present invention relates to certain substituted oxadiazole tripeptides, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, **emphysema.** HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors.

  Excerpt(s): The serine proteases are a class of enzymes, which includes elastase, chymotrypsin, cathepsin G, trypsin and thrombin. These proteases have in common a catalytic triad consisting of Serine-195, Histidine-57 and Aspartic acid-102 (chymotrypsin numbering system). Human neutrophil elastase (HNE) is a proteolytic enzyme secreted by polymorphonuclear leukocytes (PMNs) in response to a variety of inflammatory stimuli. This release of HNE and its extracellular proteolytic activity are highly regulated and are normal, beneficial functions of PMNs. The degradative capacity of HNE, under normal circumstances, is modulated by relatively high plasma concentrations of.alpha.sub.1 -proteinase inhibitor (.alpha.sub.1 -PI). However, stimulated PMNs produce a burst of active oxygen metabolites, some of which (hypochlorous acid for example) are capable of oxidizing a critical methionine residue in.alpha.sub.1 -PI. Oxidized.alpha.sub.1 -PI has been shown to have limited potency as an HNE inhibitor and it has been proposed that alteration of this protease/antiprotease balance permits HNE to perform its degradative functions in localized and controlled environments. Despite this balance of protease/antiprotease activity, there are several human disease states in which a breakdown of this control mechanism is implicated in the pathogenesis of the condition. Improper modulation of HNE activity has been suggested as a contributing factor in adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement of PMNs and neutrophil elastase in myocardial ischemia-reperfusion injury. Humans with below-normal levels of.alpha.sub.1 -PI have an increased probability of developing **emphysema.** HNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulonephritis, dermatitis, psoriasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors. There is a need for effective inhibitors of HNE as therapeutic and as prophylactic agents for the treatment and/or prevention of elastase-mediated problems.

Web site: http://www.delphion.com/details?pn=US06001813__

Patent Applications on Emphysema

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 emphysema:

- **1,3,4-Oxadiazolin-2-one derivatives and drugs containing these derivatives as the active ingredient**

  Inventor(s): Ohmoto, Kazuyuki; (Mishima-gun, JP), Okuma, Motohiro; (Mishima-gun, JP), Sekioka, Tomohiko; (Mishima-gun, JP)

  Correspondence: SUGHRUE MION, PLLC; 2100 PENNSYLVANIA AVENUE, N.W.; WASHINGTON; DC; 20037; US

  Patent Application Number: 20030087831

  Date filed: May 31, 2002

  Abstract: 1The compounds of formula (I) have an elastase inhibitory activity, therefor, they are useful for the treatment and/or prevention of a disease induced by an abnormal enhancement of degradation of elastin, collagen fiber and/or proteoglycans by elastase, for example, pulmonary **emphysema,** rheumatoid arthritis, arteriosclerosis, adult respiratory distress syndrome, myocardial infarction, ulcerative colitis and gingivitis.

  Excerpt(s): (3) a pharmaceutical composition comprising them as active ingredient. Recently, researches and developments concerning elastase inhibitors are becoming active. was disclosed.

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

- **ANTI-INFLAMMATORY PEPTIDES DERIVED FROM C-REACTIVE PROTEIN**

  Inventor(s): FRIDKIN, MATITYAHU; (REHOVOT, IL), YAVIN, ERAN J.; (REHOVOT, IL)

  Correspondence: BROWDY & NEIMARK; 624 NINTH STREET, N.W.; SUITE 300; WASHINGTON; DC; 20001; US

  Patent Application Number: 20020119917

  Date filed: January 27, 1999

  Abstract: A peptide corresponding to positions 89-96 of the human C-reactive protein (CRP) of the formula: Val.sub.89-Thr-Val-Ala-Pro-Val-His-Ile.sub.96 and modifications thereof obtained by substitution, elongation, amidation of the C-terminal or acylation of the N-terminal, inhibit in vitro the enzymatic activity of human leukocyte elastase (hLE) and/or of human leukocyte cathepsin G(hCG) and can be used for the treatment of chronic inflammation conditions such as rheumatoid arthritis, pulmonary **emphysema** and cystic fibrosis.

---

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

Excerpt(s): The present invention relates to synthetic peptides derived from the primary sequence of the acute phase reactant C-reactive protein (CRP), which peptides inhibit in vitro the enzymatic activities of human leukocyte elastase (hLE) and human leukocyte cathepsin G (hCG), two potent serine proteases associated with tissue damage occurring in the course of several chronic inflammatory conditions. The invention further relates to anti-inflammatory pharmaceutical compositions comprising said CRP-derived peptides. The following abbreviations will be used throughout the specification: CRP, C-reactive protein; hLE, human leukocyte elastase; hCG, human leukocyte cathepsin G;.alpha.sub.1-PI,.alpha.sub.1-protease inhibitor; ACT,.alpha.-antichymotrypsin; MeOSuc-AAPV-NA, methoxysuccinyl-Ala-Ala-Pro-Val-nitroanilide; Suc-AAPF-NA, succinyl-Ala-Ala-Pro-Phe-nitroanilide. C-reactive protein (CRP) is a plasma protein classified as a major acute phase reactant due to its dramatic accumulation in the blood stream during the inflammatory response. Within a relatively short period (24-48 hr) following tissue injury or certain traumatic events, the CRP blood concentration may rise 1000-fold over the normal level to as high as 1 mg/mL (Ballue and Kushner, 1992).

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

- **BIOCOMPATIBLE GLUE**

  Inventor(s): JOHANSSON-RUDEN, GUNILLA; (ASKIM, SE), SODERSTROM, BENGT; (GOTEBORG, SE)

  Correspondence: WHITE & CASE LLP; PATENT DEPARTMENT; 1155 AVENUE OF THE AMERICAS; NEW YORK; NY; 10036; US

  Patent Application Number: 20020045919

  Date filed: July 17, 1997

  Abstract: Use of one or more saccharides, for example one or more non-toxic mono-, di-, tri-, oligo- or polysaccharides, in the manufacture of a biocompatible glue for adhering a first structure to a surface of a second structure. The biocompatible glue can be adapted to act as a temporary glue. In this case the glue may be used to enable a medical structure to be transferred from a medical instrument onto the surface of a structure of a human or animal body, for example as in the transfer of a buffer material from the fork of a surgical stapler to a diseased lung after one or more rows of staples have been fired through the buffer material into the lung during lung volume reduction surgery for treating **emphysema.** The biocompatible glue can also to advantage be used to adhere or secure medical structures to a structure of a human or animal body direct, such as in the case of a patch being applied to the skin of a mammal.

  Excerpt(s): The present invention relates to a new use of a known material in the manufacture of a biocompatible glue for adhering a first structure to a surface of a second structure, the invention having particular, although not exclusive, application in surgery or other medical procedures such as lung volume reduction for treatment of **emphysema** or treating a bodily organ or tissue. It also relates to a medical device comprising a patch of polymeric material provided with a coating of such a glue. Emphysema is a condition of the lung characterised by the lung capacity tending to decrease. After a patient has contracted the disease typically only 15 to 20 per cent of the normal lung capacity can remain. To improve the lung capacity around about 30 per cent of the lung volume is cut off by trimming away part of the lung in a procedure known as lung volume reduction surgery to help the healthy tissue to expand and thus improve lung capacity. The usual way of achieving this is by using a linear surgical stapler to place two rows of closely spaced staples along the line of the desired cut and

then cutting along the line of staples. This is generally done between the rows although it may also be done on the diseased side of the lung close to one of the rows. This process may be performed several times until the most affected part of the lung has been completely cut away. When lung volume reduction surgery or other lung surgical procedures are performed a common complication is persistent air leaks which result in a significant and prolonged air loss from the lung. This has been reported to be mainly through the staple holes which can expand or tear when the lung is re-inflated.

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

- **Carbon monoxide as a biomarker and therapeutic agent**

  Inventor(s): Choi, Augustine M.; (Guilford, CT), Lee, Patty J.; (Guilford, CT), Leo, Otterbein E.; (Hamden, CT)

  Correspondence: JANIS K. FRASER, PH.D., J.D.; Fish & Richardson P.C.; 225 Franklin Street; Boston; MA; 02110-2804; US

  Patent Application Number: 20020155166

  Date filed: January 15, 2002

  Abstract: The present invention relates to the use of carbon monoxide (CO) as a biomarker and therapeutic agent of heart, lung, liver, spleen, brain, skin and kidney diseases and other conditions and disease states including, for example, asthma, **emphysema,** bronchitis, adult respiratory distress syndrome, sepsis, cystic fibrosis, pneumonia, interstitial lung diseases, idiopathic pulmonary diseases, other lung diseases including primary pulmonary hypertension, secondary pulmonary hypertension, cancers, including lung, larynx and throat cancer, arthritis, wound healing, Parkinson's disease, Alzheimer's disease, peripheral vascular disease and pulmonary vascular thrombotic diseases such as pulmonary embolism. CO may be used to provide anti-inflammatory relief in patients suffering from oxidative stress and other conditions especially including sepsis and septic shock. In addition, carbon monoxide may be used as a biomarker or therapeutic agent for reducing respiratory distress in lung transplant patients and to reduce or inhibit oxidative stress and inflammation in transplant patients.

  Excerpt(s): This application claims priority from provisional application No. 60/127,616, filed Apr. 1, 1999. Heme oxygenase (HO) catalyzes the first and rate limiting step in the degradation of heme to yield equimolar quantities of biliverdin IXa, carbon monoxide (CO), and iron (Choi, et al., Am. J. Respir. Cell Mol. Biol. 15: 9-19; and Maines, Annu. Rev. Pharmacol. Toxicol. 37: 517-554). Three isoforms of HO exist; HO-1 is highly inducible while HO-2 and HO-3 are constitutively expressed (Choi, et al., supra, Maines, supra and McCoubrey, et al., E. J. Bioch. 247: 725-732). Although heme is the major substrate of HO-1, a variety of non-heme agents including heavy metals, cytokines, hormones, endotoxin and heat shock are also strong inducers of HO-1 expression (Choi, et al., supra, Maines, supra and Tenhunen, et al., J. Lab. Clin. Med. 75: 410-421). This diversity of HO-1 inducers has provided further support for the speculation that HO-1, besides its role in heme degradation, may also play a vital function in maintaining cellular homeostasis. Furthermore, HO-1 is highly induced by a variety of agents causing oxidative stress including hydrogen peroxide, glutathione depletors, UV irradiation, endotoxin and hyperoxia (Choi, et al., supra, Maines, supra and Keyse, et al., Proc. Natl. Acad. Sci. USA. 86: 99-103). One interpretation of this finding is that HO-1 can serve as a key biological molecule in the adaptation and/or defense against oxidative stress (Choi, et al., supra, Lee, et al., Proc Natl Acad Sci USA 93: 10393-10398;

Otterbein, et al., Am. J. J. Respir. Cell Mol. Biol. 13: 595-601; Poss, et al., Proc. Natl. Acad. Sci. USA. 94: 10925-10930; Vile, et al., Proc. Natl. Acad. Sci. 91: 2607-2610; Abraham, et al., Proc. Natl. Acad. Sci. USA. 92: 6798-6802; and Vile and Tyrrell, J. Biol. Chem. 268: 14678-14681. Our laboratory and others have shown that induction of endogenous HO-1 provides protection both in vivo and in vitro against oxidative stress associated with hyperoxia and lipopolysaccharide-induced tissue injury (Lee, et al., supra, Otterbein, et al., supra and Taylor, et al., Am. J Physiol. 18: L582-L591). We have also shown that exogenous administration of HO-1 via gene transfer can provide protection against oxidant tissue injury and elicit tolerance to hyperoxic stress (Otterbein, et al., Am. J. Resp. Crit. Care Med. 157: A565 (Abstr)).

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

- **COMPOSITION, FORMULATIONS & METHOD FOR PREVENTION & TREATMENT OF DISEASES AND CONDITIONS ASSOCIATED WITH BRONCHOCONSTRICTION, ALLERGY(IES) & INFLAMMATION**

  Inventor(s): NYCE, JONATHAN W.; (PRINCETON, NJ)

  Correspondence: VIVIANA AMZEL, PH.D.; EpiGenesis Pharmaceuticals, Inc.; 7 Clarke Drive; Cranbury; NJ; 05812; US

  Patent Application Number: 20030087845

  Date filed: June 9, 1998

  Abstract: A pharmaceutical composition effective for preventing and alleviating bronchoconstriction, allergy(ies) and/or inflammation comprises a surfactant and a nucleic acid comprising an oligonucleotide anti-sense to an adenosine A1, A2a, A2b or A3 receptor gene, mRNA, flanking regions or regions bridging the intro/exon borders, analogues which bind thymidine but have low adenosine content or exhibit lower or no adenosine receptor agonist activity, combinations thereof, physiologically acceptable salts thereof or mixtures thereof, and optionally a carrier and other agents such as therapeutic agents and formulation products known in the art. The composition is formulated for administration by a multiplicity of routes for the prevention or alleviation of diseases and conditions associated with breathing difficulties, impeded and obstructed airways, bronchoconstriction, allergy and/or inflammation. Among the appplications of this technology are the prevention and treatment of diseases and conditions such as asthma, kidney damage or failure, ARDS, pulmonary vasoconstriction, inflammation, allergies, impeded respiration, respiratory distress syndrome, pain, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, **emphysema,** chronic obstructive pulmonary disease (COPD), and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, lung cancer, pancreatic cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic, lung, breast, and prostate metastases, etc., to counter the renal damage and failure associated with ischemic conditions and the administration of certain drugs and radio active diagnostic and therapeutic agents, as well as a joint therapy with the administration of adenosine and adenosine-like agents in the treatment of arrhythmias such as SVT and in cardiovascular function tests (stress tests). The present agent(s) is (are) also suitable for administration before, during and after other treatments, including radiation, chemotherapy, antibody therapy, phototherapy and cancer, and other types of surgery. Alternatively, the present agent may be effectively administered preventatively, prophylactically or therapeutically, and in conjunction with other

therapies, or by itself for conditions without known therapies or as a substitute for therapies that have significant negative side effects.

Excerpt(s): This invention relates to compositions and formulations of oligonucleotides and surfactants, which are highly effective for the prevention and treatment of diseases and conditions associated with difficult breathing, bronchoconstriction, impeded airways, allergy(ies) and inflammation of the lungs. Adenosine A.sub.1-mediated diseases and conditions, such as asthma and Acute Respiratory Distress Syndrome (ARDS), among others, are common diseases in industrialized countries, and in the United States alone account for extremely high health care costs. These diseases or conditions have recently been increasing at an alarming rate, both in terms of prevalence and mortality. Occupational asthma is predicted to be the preeminent occupational lung disease in the next decade. In many of these, the underlying causes remain poorly understood. Adenosine, a natural nucleoside, may constitute an important natural mediator of bronchial asthma and ARDS. The potential role of adenosine in these diseases or conditions is supported by experimental findings that, for example and in contrast to normal individuals, asthmatics respond to aerosolized adenosine with marked bronchoconstriction. Similarly, asthmatic rabbits produced using the dust mite allergic rabbit model of human asthma also were shown to respond to aerosolized adenosine with marked bronchoconstriction, while non-asthmatic rabbits showed no response. Recent work using this model system has suggested that adenosine-mediated bronchoconstriction in asthma is mediated through the stimulation of the adenosine A.sub.1 receptor. Other experimental data suggest the possibility that adenosine receptors may also be involved in allergic and inflammatory responses.

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

- **Compositions and methods for treating emphysema**

  Inventor(s): Ingenito, Edward; (Kingston, MA)

  Correspondence: FISH & RICHARDSON PC; 225 FRANKLIN ST; BOSTON; MA; 02110; US

  Patent Application Number: 20030181356

  Date filed: March 11, 2003

  Abstract: The present invention features compositions and methods for treating **emphysema** by reducing the amount of force the fibers in the lung (e.g., the collagen and elastin fibers in the walls of the alveoli) must bear. More particularly, in one embodiment, the invention features a pharmaceutically acceptable composition comprising a lipid that, when applied to an enlarged alveolus (e.g., an alveolus having a diameter substantially larger than (e.g., 5, 10, 20, 50, or 100% or more than) the average alveoli in a healthy patient (i.e., a patient with no discernable lung disease), exerts a surface tension within the alveolus that substantially reduces the stress on fibers within the alveolus when inflated by a normal inspiration. The composition can display a.gamma.* of about 30 to about 70 dynes/cm.

  Excerpt(s): This application claims the benefit of the filing date of U.S. Ser. No. 60/363,118, which was filed on Mar. 11, 2002. The contents of the prior provisional application is hereby incorporated by reference in its entirety. This invention features compositions and methods for treating patients who have certain lung diseases, such as **emphysema.** Emphysema, together with asthma and chronic bronchitis, represent a disease complex known as chronic obstructive pulmonary disease (COPD). These three

diseases are related in that they each cause difficulty breathing and, in most instances, they progress over time. There are substantial differences, however, in their etiology, pathology, and prognosis. For example, while asthma and chronic bronchitis are diseases of the airways, **emphysema** is associated with irreversible, destructive changes in lung parenchyma distal to the terminal bronchioles. Cigarette smoking is the primary cause of **emphysema;** the smoke triggers an inflammatory response within the lung, which is associated with an activation of both elastase and matrix metallo-proteinases (MMPs). These enzymes degrade key proteins that make up the tissue network of the lungs (Shapiro et al., Am. J. Resp. Crit. Care Med. 160:s29-s32, 1999; Hautamaki et al., Science 277:2002-2004). In fact, the pathological determinant of lung dysfunction in **emphysema** seems to be the progressive destruction of elastic tissue, which causes loss of lung recoil and progressive hyper-expansion.

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

- **Devices for creating collateral channels in the lungs**

  Inventor(s): Laufer, Michael D.; (Menlo Park, CA), Roschak, Ed; (Mountain View, CA), Tanaka, Don; (Saratoga, CA)

  Correspondence: MORRISON & FOERSTER LLP; 755 PAGE MILL RD; PALO ALTO; CA; 94304-1018; US

  Patent Application Number: 20020049370

  Date filed: July 18, 2001

  Abstract: The devices and methods disclosed herein are directed to altering gaseous flow within a lung to improve the expiration cycle of, for instance, an individual having Chronic Obstructive Pulmonary Disease. More particularly, these devices and methods produce and to maintain collateral openings or channels through the airway wall so that expired air is able to pass directly out of the lung tissue to facilitate both the exchange of oxygen ultimately into the blood and/or to decompress hyper-inflated lungs. The devices and methods also disclose locating and selecting a site for creation of a collateral opening.The invention is directed to methods and devices to altering gaseous flow within a lung to improve the expiration cycle of an individual, particularly individuals having Chronic Obstructive Pulmonary Disease (COPD). More particularly, methods and devices are disclosed to produce and to maintain collateral openings or channels th rough the airway wall so that expired air is able to pass directly out of the lung tissue to facilitate both the exchange of oxygen ultimately into the blood and/or to decompress hyper-inflated lungs.The term "Chronic Obstructive Pulmonary Disease" (COPD) is generally used to describe the disorders of **emphysema** and chronic bronchitis. Previously, COPD was also known as Chronic Obstructive Lung Disease (COLD), Chronic Airflow Obstruction (CAO), or Chronic Airflow Limitation (CAL). Some also consider certain types of asthma to fall under the definition of COPD. **Emphysema** is characterized by an enlargement of air spaces inside the lung. Hence, **Emphysema** is an anatomic definition and it can only be presumed in a living patient. Chronic bronchitis is characterized by excessive mucus production in the bronchial tree. Chronic bronchitis is a clinical definition and denotes those individuals who meet criteria defining the disease. It is not uncommon for an individual to suffer from both disorders.

  Excerpt(s): In 1995, the American Lung Association (ALA) estimated that between 15-16 million Americans suffered from COPD. The ALA estimated that COPD was the fourth-ranking cause of death in the U.S. The ALA estimates that the rates of **emphysema** is 7.6 per thousand population, and the rate for chronic bronchitis is 55.7 per thousand

population. Those inflicted with COPD face disabilities due to the limited pulmonary functions. Usually, individuals afflicted by COPD also face loss in muscle strength and an inability to perform common daily activities. Often, those patients desiring treatment for COPD seek a physician at a point where the disease is advanced. Since the damage to the lungs is irreversible, there is little hope of recovery. Most times, the physician cannot reverse the effects of the disease but can only offer treatment and advice to halt the progression of the disease. To understand the detrimental effects of COPD, the workings of the lungs requires a cursory discussion. The primary function of the lungs is to permit the exchange of two gasses by removing carbon dioxide from venous blood and replacing it with oxygen. Thus, to facilitate this exchange, the lungs provide a blood gas interface. The oxygen and carbon dioxide move between the gas (air) and blood by diffusion. This diffusion is possible since the blood is delivered to one side of the blood-gas interface via small blood vessels (capillaries). The capillaries are wrapped around numerous air sacs called alveoli which function as the blood-gas interface. A typical human lung contains about 300 million alveoli.

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

- **Genes expressed in lung cancer**

  Inventor(s): Lasek, Amy K. W.; (Oakland, CA), Shyjan, Andrew W.; (San Carlos, CA), Turner, Christopher M.; (Stanford, CA)

  Correspondence: LEGAL DEPARTMENT; INCYTE GENOMICS, INC.; 3160 Porter Drive; Palo Alto; CA; 94304; US

  Patent Application Number: 20030175704

  Date filed: October 4, 2001

  Abstract: The present invention relates to a combination comprising a plurality of cDNAs which are differentially expressed in respiratory disorders and which may be used in their entirety or in part to diagnose, to stage, to treat, or to monitor the treatment of a subject with a respiratory disorder including lung cancer, chronic obstructive pulmonary disease, **emphysema,** and asthma.

  Excerpt(s): The present invention relates to a combination comprising a plurality of cDNAs which are differentially expressed in lung cancer and which may be used entirely or in part to diagnose, to stage, to treat, or to monitor the progression or treatment of respiratory disorders such as lung cancer, chronic obstructive pulmonary disease, **emphysema,** and asthma. Array technology can provide a simple way to explore the expression of a single polymorphic gene or the expression profile of a large number of related or unrelated genes. When the expression of a single gene is examined, arrays are employed to detect the expression of a specific gene or its variants. When an expression profile is examined, arrays provide a platform for examining which genes are tissue specific, carrying out housekeeping functions, parts of a signaling cascade, or specifically related to a particular genetic predisposition, condition, disease, or disorder. The potential application of gene expression profiling is particularly relevant to improving diagnosis, prognosis, and treatment of respiratory disorders. For example, the levels at which particular sequences are expressed in lung cancer may be compared with the levels and sequences expressed in lung tissue that is normal or affected by other diseases.

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

- **Intratracheal administration of lysozyme**

  Inventor(s): Cantor, Jerome Owen; (Bayside, NY), Shteyngart, Bronislava; (Brooklyn, NY)

  Correspondence: Jerome O. Cantor, MD; 12-15 Estates Lane; Bayside; NY; 11360; US

  Patent Application Number: 20010036443

  Date filed: April 5, 2001

  Abstract: The subject invention is directed to the treatment of respiratory disorders by intratracheal administration of an effective amount of lysozyme. Respiratory disorders include **emphysema,** pneumonia, respiratory distress syndrome, bronchopulmonary dysplasia, interstitial fibrosis, cystic fibrosis, and neoplasia. The treatment is intended for a variety of animals, such as premature neonates to adult humans. Administration of lysozyme may be performed by aerosol, which can be generated by a nebulizer or by instillation. The lysozyme may be administered alone or with a carrier such as saline solution, DMSO, and alcohol, or water. It may also be used as a vehicle for the intratracheal administration of drugs or other agents to the lung. The lysozyme may be isolated from a natural source, such as eggs, or synthesized by a bioprocess, such as fermentation. The effective daily amount of lysozyme is from about 10.mu.g/kg to about 1 mg/kg of body weight.

  Excerpt(s): Lysozyme is increased in inflammatory reactions and is a component of the extracellular matrix, but its possible role in lung diseases such as **emphysema** and interstitial fibrosis has not been investigated. Determining the significance of any changes in pulmonary lysozyme content is complicated by the fact that this protein has no recognized physiological function in the lung other than protecting it from bacterial infection (1-3). To further understand the role of lysozyme in pulmonary disease, tissue sections from normal, fibrotic, and emphysematous human lungs were evaluated for differences in lysozyme content. An increase in extracellular lysozyme was specifically observed in lung tissues with pulmonary **emphysema,** and the protein was preferentially associated with elastic fibers, which undergo breakdown in this disease (4). Since this laboratory and other investigators have previously shown that hyaluronan and other polysaccharides surround elastic fibers (5-7), normal lung tissues were treated with hyaluronidase and examined for their ability to bind exogenously administered lysozyme. Such treatment resulted in increased attachment of lysozyme (4), suggesting that degradation of extracellular matrix components, as occurs in pulmonary **emphysema,** may expose binding sites for lysozyme on elastic fibers. In vitro studies, using an extracellular matrix preparation mainly composed of elastic fibers, confirmed that lysozyme has a strong affinity for these fibers (unpublished observations).

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

- **Medical embolization element and method of embolizing tubular organ**

  Inventor(s): Kaji, Hinako; (Tokyo, JP), Kaji, Kunihide; (Tokyo, JP)

  Correspondence: Paul J. Esatto, Jr.; Scully, Scott, Murphy & Presser; 400 Garden City Plaza; Garden City; NY; 11530; US

  Patent Application Number: 20030018351

  Date filed: July 19, 2002

Abstract: To provide a medical embolization element for embolizing the internal cavity of a tubular organ of a subject, for example, a medical embolization element for embolizing a bronchus during treatment of lung **emphysema.** A placing object being placed in a bifurcation of the tubular cavity includes a first embolization portion capable of airtightly sealing a first branch tubular cavity of the bifurcation, a second embolization portion capable of embolizing another second branch tubular cavity of the bifurcation, and a locking portion being locked to an edge portion of the junction portion between the first and second branch tubular cavities. Other than the above described placing object, a placing object having a balloon, a placing object shaped like cap to be attached on the tip of an endoscope, a placing object expandable in the tubular organ, and a placing object solidifies in the tubular organ are disclosed.

Excerpt(s): This application is based upon and claims the benefit of priority from the prior Japanese Patent Application No. 2001-220005, filed Jul. 19, 2001, the entire contents of the application are incorporated herein by reference. The invention relates to a medical embolization element which is used in an internal cavity of a tubular organ of a subject, and more specifically, to a medical embolization element which is used for embolizing a bronchus, for example, during treatment of lung **emphysema.** In general, lung **emphysema** is a morbid change, which is mainly formed by inhalation of harmful substances due to smoking or the like and mainly features wide destruction in peripheral airways and alveoli. The formation of such morbid change is chronic and progressive, and the respiratory function of a patient whose lung **emphysema** is in an advanced stage is disordered to a remarkable extent. As the basic elements of disfunction of respiratory disorder due to lung **emphysema,** there are a reduction in resiliency due to destruction of alveoli and a decrease in the area of a functional alveolar membrane. A plurality of elements of disfunction are combined with these basic elements of disfunction to cause a reduction in ventilation efficiency and a decrease in potential ability of breathing, resulting in respiratory disorder.

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

- **Method of detecting inflammatory lung disorders**

  Inventor(s): Rastelli, Luca; (Guilford, CT), Smithson, Glennda; (Branford, CT)

  Correspondence: Ivor R. Elrifi; MINTZ, LEVIN, COHN, FERRIS,; GLOVSKY and POPEO, P.C.; One Financial Center; Boston; MA; 02111; US

  Patent Application Number: 20020115626

  Date filed: May 25, 2001

  Abstract: Disclosed are methods of detecting and treating inflammatory lung disorders, such as **emphysema,** asthma bronchitis or allergy. Also disclosed are methods of identifying agents for treating inflammatory lung disorders.

  Excerpt(s): This application claims priority from U.S. Ser. No. 60/207,104, filed May 5, 2000 which is incorporated by reference in its entirety. The invention relates to methods of detecting inflammatory lung disorders. Antileukoproteases, also known as secretory leukocyte protease inhibitors, are a class of acid-stable proteinase inhibitors with strong affinity for trypsin and chymotrypsin as well as for neutrophil lysosomal elastase and cathepsin G. Antileukoproteases are present in mucous fluids such as seminal plasma, cervical mucus, bronchial and nasal secretions, and tears.

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

- **Methods and apparatuses for analyzing images**

  Inventor(s): Hoffman, Eric A.; (Iowa City, IA), McLennan, Geoffrey; (Iowa City, IA), Mitsa, Theophano; (Waukesha, WI), Sonka, Milan; (Iowa City, IA), Uppaluri, Renuka; (Iowa City, IA)

  Correspondence: FULLBRIGHT & JAWORSKI L.L.P.; 600 CONGRESS AVE.; SUITE 2400; AUSTIN; TX; 78701; US

  Patent Application Number: 20030103665

  Date filed: September 20, 2002

  Abstract: A method and apparatus for analyzing CT images to determine the presence of pulmonary tissue pathology, such as in **emphysema,** IPF, sarcoid, etc. In accordance with one embodiment, a CT slice is selected to perform an automated, objective, and quantitative analysis of the slice. Initially, an image processing stage is performed, which includes segmentation and edgementation of the selected CT slice for preparation of a series of objective, quantitative measures to be performed on the slice. A region of interest (ROI) is selected on the CT slice in which these objective, quatitative measures are to be taken. The first set of objective, quantitative measures are first order texture measures that describe a frequency of occurrence of all gray levels assigned to pixels within the ROI of the image slice. The second set of objective, quantitative measures are second order texture measures that characterize the spatial interdependencies between particular pixels of the ROI. Fractal analysis could also be performed to provide additional objective, quantitative measures of the ROI. The ROI is classified to a particular tissue pathology class based upon an optimal subset of first or second order texture measures and fractal measures obtained. A color-coded output is displayed for visual presentation to a user indicating the different tissue pathology classes assigned to different regions of the CT slice.

  Excerpt(s): This application claims priority of U.S. Provisional Application No. 60/037,067, filed Feb. 12, 1997, entitled: "Method and Apparatus for Analyzing CT Images to Determine the Presence of Pulmonary Parenchyma", by Renuka Uppaluri, Theophano Mitsa, Eric A. Hoffman, Geoffrey McLennan, and Milan Sonka, Atty Docket No.: IOWA:013PZ1/MOG. The present invention relates generally to the detection and diagnosis of tissue pathology using a diagnostic medical image, and, more particularly, to a method and apparatus for detecting and diagnosing the presence of pulmonary tissue pathology from CT images using an automated texture analysis procedure. Pulmonary **emphysema** is a common, debilitating, and progressive disorder of the lungs that may result from smoking. The disorder is caused by destruction of the alveolar walls of the lung parenchyma (i.e., lung tissue), which results in an abnormal enlargement of air spaces distal to the terminal bronchiole. Enlargement of these air spaces in the lungs impedes the exchange of oxygen in the air for carbon dioxide in the bloodstream. As a result of this impeded process, an individual experiences breathlessness, making ordinary tasks, once thought simple, labor intensive.

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

- **Methods and compositions for the treatment and prevention of lung disease**

  Inventor(s): Chandraratna, Roshantha A.; (Laguna Hills, CA), Massaro, Donald; (Washington, DC), Massaro, Gloria DeCarlo; (Washington, DC)

  Correspondence: Carlos A. Fisher; ALLERGAN, INC.; 2525 Dupont Drive; Irvine; CA; 92623; US

  Patent Application Number: 20010053758

  Date filed: July 31, 2001

  Abstract: Methods and compositions for the treatment of lung disease, such as **emphysema** and/or bronchopulmonary dysplasia, in a mammal. Also disclosed are methods promoting the formation of alveolar septa and increasing the gas-exchange surface area of a mammalian lung, and for the prevention and/or treatment of alveolar destruction.

  Excerpt(s): This invention concerns the use of retinoic acid receptor (RAR) antagonists for the inhibition of alveolar destruction and/or to promote the formation of alveoli in mammalian lung tissue deficient in adequate numbers of functional alveoli. Among aerobic animals, the lung functions to provide an interface for the exchange of gases between blood and the atmosphere. The agents of this exchange are numerous small sacs termed alveoli (in adult humans about 300,000,000 per lung) that provide a gas permeable-liquid impermeable barrier between the gas and liquid phases. Between the alveoli are numerous capillaries carrying deoxygenated blood to the lung from the tissues and oxygenated blood from the alveoli to the tissues. The partial pressure of oxygen in the lungs is approximately 100 mm Hg at sea level; at this pressure the binding of oxygen by hemoglobin in the erythrocytes is favored. The alveoli thus provide a means for presenting the oxygen to hemoglobin to permit the conversion of deoxyhemoglobin to hemoglobin. Because the exchange occurs at the surface of the gas/blood barrier, alveoli have evolved as a means for providing extremely high surface area in a compact overall area, thus maximizing possible gas exchange. Lack of adequate gas exchange would lead to disability which could progress to death. Diseases that result in fewer alveoli therefore are quite serious, and are common causes of inadequate oxygenation and resultant disability and death. Among such diseases are brochopulmonary dysplasia (BPD) and **emphysema.** BPD is a disease of prematurely born infants, and is characterized mainly by a failure of the infant to form a sufficient number of appropriately-sized alveoli. **Emphysema,** a disease of middle and advanced age, appears to be due to progressive proteinase-induced alveolar destruction.

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

- **Methods and compositions for treating diseases associated with excesses in ACE**

  Inventor(s): Moskowitz, David W.; (St. Louis, MO)

  Correspondence: PATREA L. PABST; HOLLAND & KNIGHT LLP; SUITE 2000, ONE ATLANTIC CENTER; 1201 WEST PEACHTREE STREET, N.E.; ATLANTA; GA; 30309-3400; US

  Patent Application Number: 20030040509

  Date filed: August 6, 2002

  Abstract: Over 40 common diseases, in addition to congestive heart failure (CHF) due to hypertension (HTN) or non-insulin dependent diabetes mellitus (type II diabetes

mellitus) (NIDDM), atherosclerotic peripheral vascular disease (ASPVD) due to HTN or NIDDM, and chronic obstructive pulmonary disease; **emphysema** (COPD), are associated with the ACE D/D genotype and should also respond to an adequate tissue-inhibitory dose of ACE inhibitors such as quinapril. Several of these diseases have now been successfully treated using higher than normal dosages of ACE inhibitors, especially hydrophobic ACE inhibitors, with good outcomes. ACE inhibitors have also been found to be useful in inhibiting apoptosis and aging in general. Dosages that have been utilized are typically greater than quinapril at a dose of 40 to 80 mg/day, i.e. up to 1 mg/kg per day for a "typical" 80 kg patient. New formulations of ACE inhibitors have been developed for these higher dosages, including 80 mg tablets, controlled and/or sustained release formulations, and formulations containing a second active agent such as a diuretic, or a compound such as furosemide 20 mg/day (for creatinine <2.5 mg/dl) or furosemide 40 mg/day (for creatinine >2.5 mg/dl), to prevent fluid retention and congestive heart failure in patients with renal failure. The ACE inhibitors can also be combined with an angiotensin receptor blocker.

Excerpt(s): This application claims priority to U.S. S. No. 60/310,064 filed Aug. 6, 2001; U.S. S. No. 60/347,905 filed Jan. 15, 2002; U.S. S. No. 60/347,013 filed Jan. 11, 2002; U.S. S. No. 60/350,563 filed Jan. 24, 2002; U.S. S. No. 60/352,484 filed Jan. 30, 2002; U.S. S. No. 60/352,072 filed Jan. 28, 2002; and U.S. S. No. 60/352,074 filed Jan. 28, 2002; U.S. S. No. 60/378,467 filed May 8, 2002; U.S. S. No. 60/379,796 filed May 13, 2002; and U.S. S. No. 60/380,741 filed May 16, 2002. The present invention is generally in the field of methods and compositions for treatment of chronic disease. Angiotensin converting enzyme (encoded by the gene DCP1, also known as ACE) catalyses the conversion of angiotensin I to the physiologically active peptide angiotensin II, which controls fluid-electrolyte balance and systemic blood pressure. Because of its key function in the renin-angiotensin system, many association studies have been performed with DCP1. Nearly all studies have associated the presence (insertion, I) or absence (deletion, D) of a 287-bp Alu repeat element in intron 16 with the levels of circulating enzyme or cardiovascular pathophysiologies. Many epidemiological studies suggest that the DCP1*D allele confers increased susceptibility to cardiovascular disease; however, other reports have found no such association or even a beneficial effect. Rieder, et al., Nat Genet 22(1):59-62 (1999), reports the complete genomic sequence of DCP1 from 11 individuals, representing the longest contiguous scan (24 kb) for sequence variation in human DNA, and identifies 78 varying sites in 22 chromosomes that resolved into 13 distinct haplotypes. Of the variant sites, 17 were in absolute linkage disequilibrium with the commonly typed Alu insertion/deletion polymorphism, producing two distinct and distantly related clades.

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

- **Methods of endobronchial diagnosis using imaging**

  Inventor(s): Kotmel, Robert; (Burlingame, CA), Perkins, Rodney; (Woodside, CA), Soltesz, Peter; (San Jose, CA), Wondka, Anthony; (Mountain View, CA)

  Correspondence: TOWNSEND AND TOWNSEND AND CREW, LLP; TWO EMBARCADERO CENTER; EIGHTH FLOOR; SAN FRANCISCO; CA; 94111-3834; US

  Patent Application Number: 20030055331

  Date filed: September 11, 2002

  Abstract: Devices and methods are provided for acquiring and analyzing an image data file to generate diagnostic information reflecting an individual lung compartment. A

lung compartment could be an entire lobe, a segment or a subsegment and beyond, hereinafter subsegments and beyond will be referred to simply as segments. Such analysis is used to assess the level of disease of individual lung compartments, both for quantification of the disease state and for determining the most appropriate treatment plan. This analysis allows the imaging technology to be used as a functional diagnostic tool as well as an anatomical diagnostic tool. To this end, dynamic data or images may also be acquired at specific points throughout the breathing cycle. Since air movement in and out of a lung compartment during the breathing cycle is a direct indicator of lung function in some diseases like **emphysema,** analysis of images during the breathing cycle will indicate levels of disease. Thus, a physician may be able to determine the nature of the disease, severity of the disease and the most effective course of treatment from a computerized image of the lung.

Excerpt(s): This application claims the benefit and priority of U.S. Provisional Patent Application No. 60/322,366 (Attorney Docket 017534-001900US), filed Sep. 11, 2001, the full disclosure of which is hereby incorporated by reference for all purposes. The present invention relates generally to medical methods, systems, and kits. Particularly, the present invention relates to methods and apparatus for performing diagnostic testing on individual compartments of a lung. More particularly, the present invention provides for such testing with imaging technologies. Chronic obstructive pulmonary disease (COPD) is a significant medical problem affecting 16 million people or about 6% of the U.S. population. Specific diseases in this group include chronic bronchitis, asthmatic bronchitis, and **emphysema.** In general, two types of diagnostic tests are performed on a patient to determine the extent and severity of COPD: 1) imaging tests and 2) functional tests. Imaging tests provide a good indicator of the location, homogeneity and progression of the diseased tissue. Images may be obtained by any standard imaging technique, such as computed tomography (CT), magnetic resonance imagining (MRI), polarized gas MRI, ultrasound, ultrasound with perfluroban, x-ray, or positive emission tomography (PET), to name a few. These imaging techniques generate a three-dimensional image of a body part, such as the lung, comprised of computerized data which can be stored, analyzed, manipulated and transmitted for a variety of uses. For example, during CT imaging, a CT scanner provides an x-ray source which rotates around the patient and each rotation produces a single cross-sectional image of a slice of the body. Incremental advancement of the patient allows a series of cross-sectional images to be taken which, when combined, create the three-dimensional image the body and the body part of interest. With some CT scanners, a scan of the lungs can be achieved in approximately 22 seconds with thin slices each in the range of 2.5 to 5.0 mm.

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

- **Methods to treat alpha1-antitrypsin deficiency**

  Inventor(s): Marcus, Nancy; (St. Louis, MO), Perlmutter, David H.; (St. Louis, MO)

  Correspondence: MORRISON & FOERSTER LLP; 3811 VALLEY CENTRE DRIVE; SUITE 500; SAN DIEGO; CA; 92130-2332; US

  Patent Application Number: 20020006909

  Date filed: January 22, 2001

  Abstract: Inhibitors of glucosidase, especially those related to castanospermine, are effective in preventing or ameliorating conditions such as liver damage and **emphysema** that are present in individuals who produce a mutant form of antitrypsin,.alpha.1-ATZ. Also effective in the method of the invention are imino sugars and their reduced forms

in general as well as phenylbutyric acid. These compounds enhance the secretion of the mutant form, which retains substantial biological activity, and do not impair its degradation in the endoplasmic reticulum.

Excerpt(s): This application claims priority under 35 U.S.C.sctn. 119(e) to provisional application No. 60/177,472 filed Jan. 21, 2000 and to application No. 60/177,392 filed Jan. 20, 2000. The contents of these applications are incorporated herein by reference. The invention relates to treatment of.alpha.1-antitrypsin (.alpha.1-AT) deficiency in individuals containing a mutant form of.alpha.1-AT exhibiting symptoms of, or at-risk for, liver damage and/or **emphysema.** In particular, the invention concerns the use of inhibitors of glucosidase and in some instances, of mannosidase in ameliorating these conditions. The enzyme.alpha.1-antitrypsin (.alpha.1-AT) is important in maintaining the condition of lung tissue by virtue of its ability to inhibit neutrophil elastase. If this elastase inhibitor is lacking in the lungs, lung diseases such as **emphysema** can develop. A substantial number of individuals are deficient in this important enzyme by virtue of the presence of a mutant form of the glycoprotein, designated.alpha.1-ATZ, differing from the wild type by a single amino acid substitution. Although.alpha.1-ATZ this retains approximately 80% of the functional activity of the wild type in inhibiting neutrophil elastase, because it is misfolded and polymerized in the endoplasmic reticulum (ER) of liver cells rather than excreted into the extracellular fluid, it exerts a hepatotoxic effect, especially in infants and children, and is not available in the lungs to carry out its function. There are, however, known pathways for degradation of the mutant.alpha.1-ATZ in the ER--one involving the sequence of stable binding to calnexin, conjugation of ubiquitin to the cytoplasmic tail of the complexed calnexin and degradation of the resulting complex by the proteasome (Qu, D., et al., J. Biol. Chem. (1996) 271:22791-22795). There is also a ubiquitin-independent proteasomal mechanism (Teckman, J. H., et al., Biochem J. (1986) 236:853-860).

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

- **Methods, compositions and modes of delivery for the treatment of emphysema using 13-cis-retinoic acid**

  Inventor(s): Belloni, Paula N.; (Half Moon Bay, CA)

  Correspondence: PENNIE & EDMONDS, LLP; 1155 Avenue of the Americas; New York; NY; 10036-2711; US

  Patent Application Number: 20020049252

  Date filed: September 26, 2001

  Abstract: The current invention is directed to methods of treating or preventing **emphysema,** pharmaceutical compositions suitable for the treatment or prevention of **emphysema** and methods for delivering formulations into the lung of a mammal suffering from **emphysema.**More generally, the invention encompasses the use of 13-cis-retinoic acid to treat or prevent certain chronic obstructive airway disorders, particularly chronic obstructive pulmonary disease including chronic bronchitis, **emphysema** and asthma in mammals, especially humans that smoke or smoked cigarettes. In another aspect, the present invention encompasses the use of pharmaceutical compositions of 13-cis-retinoic acid to treat **emphysema.** Moreover, the current invention encompasses the use of electrohydrodynamic aerosol devices, aerosol devices and nebulizers to deliver formulations of 13-cis-retinoic acid into the lung of a mammal suffering from **emphysema.** The invention also encompasses the systemic use as well as the local use of 13-cis-retinoic acid. In a another aspect the current invention encompasses a

pharmaceutical composition for preventing **emphysema** in a human at risk of **emphysema** through administration of a amount of 13-cis-retinoic acid, or a pharmaceutically acceptable salt, hydrate, solvate, or pro-drug thereof in a pharmaceutically acceptable carrier, that is sufficient to prevent **emphysema.**

Excerpt(s): The invention relates to methods of treating **emphysema** with 13-cis-retinoic acid, pharmaceutical compositions of 13-cis-retinoic acid useful in the treatment of **emphysema** and methods for delivering formulations of 13-cis-retinoic acid to the lung of a mammal suffering from **emphysema.** 13-cis-retinoic acid is also known as isotretinoin, AGN 190013, Neovitamin A acid, Ro-4-3780, 13-cis-.beta.-Retinoic acid and 13-cis-Vitamin A acid. 13-cis-retinoic acid is sold under the tradenames Accutane.RTM., Roaccutan.RTM. and Roaccutane.RTM. for the treatment of severe recalcitrant nodular acne (Physicians' Desk Reference 54.sup.th Ed., p. 2610, 2000; Peck et al., N. Eng. J. Med.; Peck et al., U.S. Pat. No. 5,698,593). 13-cis-Retinoic acid has also been reported to be effective in treating psychotic illnesses such as schizophrenia (Straw, U.S. Pat. No. 4,808,630) and cancer of head, neck and lung (Tomas et al., Annals of Oncology, 1999, 10, 95; Benner et al., Seminars in Hematology, 1994, 31, 26). 13-cis-Retinoic acid is currently in clinical trials for treatment of these forms of cancer at a number of locations (e.g., University of Texas SW Medical Center, Dallas Tex.; University of Texas MD Anderson Cancer Center, Houston, Tex.; Department of Veteran Affairs Medical Center, Temple, Tex.). 13-cis-retinoic acid is a member of the retinoid class of compounds which are structural analogues of vitamin A and include both natural and synthetic compounds. Naturally occurring retinoid compounds such as all trans retinoic acid ("ATRA"), 9-cis-retinoic acid, trans 3-4 didehydroretinoic acid, 4-oxo retinoic acid and retinol are pleiotrophic regulatory compounds that influence a large number of inflammatory, immune and structural cells.

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

- **Mutant plasminogen activator-inhibitor type 1 (PAI-1) and uses thereof**

  Inventor(s): Lawrence, Daniel A.; (Derwood, MD), Stefansson, Steingrimor P.; (Gaithersburg, MD)

  Correspondence: FOLEY AND LARDNER; SUITE 500; 3000 K STREET NW; WASHINGTON; DC; 20007; US

  Patent Application Number: 20030216321

  Date filed: September 30, 2002

  Abstract: Mutants of the human PAI-1 protein are described which are inhibitors of neutrophil elastase or are inhibitors of vitronectin (Vn)-dependent cell migration. These mutants preferably comprise one or two amino acid substitutions in the reactive center loop of PAI-1, particularly at positions 331 and 346 of the mature protein. These mutants are notable in being resistant to inactivation by elastase, having high affinity for Vn, or both properties. These mutant proteins as pharmaceutical compositions are used to inhibit elastase in a subject, thereby treating a number of disorders associated with elastase activity, most notatably **emphysema,** ARDS, inflammatory lung injury and cystic fibrosis. The mutants which interact with Vn are used to inhibit cell migration in a subject, thereby treating diseases or conditions associated with undesired cell migration and proliferation, particularly of smooth muscle cells. Such conditions include atherosclerosis, post angioplasty restenosis, fibrosis associated with chronic inflammation or chemotherapy, tumor invasion and metastasis and conditions in which angiogenesis is pathogenic. Also disclosed are peptides of such mutant proteins,

mutant-specific antibodies, nucleic acid molecules, particularly DNA, encoding the mutant protein and host cells transformed by such nucleic acids.

Excerpt(s): The invention in the field of biochemistry and medicine relates to compositions comprising mutant proteins of plasminogen activator inhibitor-type 1 (PAI-1) which have the capacity to inhibit the enzyme elastase and to inhibit vitronectin (Vn)-dependent migration of cells. This invention also relates to uses of these proteins for the treatment of diseases and disorders associated with elastase activity or in which migration and migration-driven proliferation of cells have pathophysiologic consequences. Plasminogen activators (PAs) are specific serine proteinases that activate the proenzyme plasminogen, by cleavage of a single Arg-Val peptide bond, to the enzyme plasmin (Saksela O, Biochim Biophys Acta (1985) 823:35-65). Two plasminogen activators are found in mammals, tissue-type PA (tPA) and urokinase-type PA (uPA) (Saksela O et al, Annu Rev Cell Biol (1988) 4:93-126). These enzymes are thought to influence critically many biological processes, including vascular fibrinolysis (Bachmann E, Thromb Haemost (1987) 10:227-265), ovulation (Hsuch A J W et al, In: Haseltine F P et al, eds, Meiotic Inhibition: Molecular Control of Meiosis New York: Liss 1988:227-258), inflammation (Pollanen J et al., Adv Cancer Res (1991) 57:273-328), tumor metastasis (Dano K et al., Adv Cancer Res (1985) 44:139-266), angiogenesis (Moscatelli D et al., Biochim Biophys Acta (1988) 948:67-85), and tissue remodeling (Saksela, supra). The regulation of PAs is a complex process controlled on many levels. The synthesis and release of PAs are governed by various hormones, growth factors, and cytokines (Saksela, supra; Dano et al., supra). Following secretion, PA activity can be regulated both positively and negatively by a number of specific protein-protein interactions. Activity can be enhanced or concentrated by interactions with fibrin (Hoylaerts M et al., J Biol Chem (1982) 257:2912-2919), the uPA receptor (uPAR) (Ellis V et al., Semin Thromb Hemost (1991) 17:194-200), the tPA receptor (tPAR) (Hajjar K A et al., J Biol Chem (1990) 265:2908-2916), or the plasminogen receptor (Plow E F et al., Thromb Haemost (1991) 66:32-36).

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

- **Oral Mugwort-moxibustion pipe**

  Inventor(s): Un Mam, Ko; (Seoul, KR)

  Correspondence: Un Mam KO; 396-7 Ma Po-Dong; Ma Po-Ku, Seoul; KR

  Patent Application Number: 20020069887

  Date filed: August 16, 2001

  Abstract: Mugwart-moxibustion is widely used for curing many diseases in Asian countries. However, because of constraints on its usage, it could not be applied to the respiratory system. To solve this problem, this invention was devised. Through the use of a smoking pipe stuffed with mugwart, respiratory disease, such as inflammation, pharyngitis, and **emphysema,** can be cured. The embodiment of the invention, "Oral Mugwart-moxibustion pipe", is comprised of three parts. One is a mouth filter for filtering harmful substances. The second is a connecting pipe to link the mouth filter and smoking part. The other is smoking part to hold mugwort to be smoldered.

  Excerpt(s): This application claims the benefit of patent application number 20-0214486, filed Dec. 11, 2000, in the Korea Intellectual Property Office ("KIPO") for an invention having the above-stated title. As-filed KIPO patent application number 20-0214486 ("Foreign Application") is hereby incorporated herein by reference. The English

language translation of the Foreign Application is the remainder of this document, and the Translator' s Declaration applies to the remainder of this document. The invention relates to Mugwort-moxibustion. Mugwort-moxibustion is a traditional oriental therapy. (A detailed explanation of Mugwort-moxibustion will follow in the next section) The purpose of the invention is to apply Mugwort-moxibustion to the respiratory system through the use of a smoking pipe. This invention, "Oral Mugwort-moxibustion Pipe", is comprised of a mouth filter, a connecting pipe, and smoking part. This therapy is known to originate from China and India over 2,000 years ago. In "Hwangjaenakyung", the most famous old Chinese medical book, it is explained in detail. In Asian countries, especially around China and India, Mugwart-moxibustion is utilized as a popular treatment for various diseases along with acupuncture.

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

- **Pyrimidine carboxamides useful as inhibitors of pde4 isozymes**

  Inventor(s): Chambers, Robert James; (Mystic, CT), Magee, Thomas Victor; (Mystic, CT), Marfat, Anthony; (Mystic, CT)

  Correspondence: PFIZER INC.; PATENT DEPARTMENT, MS8260-1611; EASTERN POINT ROAD; GROTON; CT; 06340; US

  Patent Application Number: 20030144300

  Date filed: July 24, 2002

  Abstract: Compounds of formula (1.0.0) are described, as well as the usefulness of a pharmaceutical composition for treating inflammatory, respiratory and allergic diseases and conditions, especially asthma; chronic obstructive pulmonary disease (COPD) including chronic bronchitis, **emphysema,** and bronchiectasis; chronic rhinitis; and chronic sinusitis.

  Excerpt(s): Reference is made to copending International application and US application based thereon, Serial No. PCT/IB98/00315, both filed Mar. 10, 1998 (Attorney Docket No. PC9762A), and published as WO 98/45268 on Oct. 15, 1998; claiming priority from application Ser. No. 60/043,403 filed Apr. 4, 1997 (Attorney Docket No. PC9762), now abandoned; which discloses nicotinamide derivatives having biological activity as inhibitors of the PDE4 isozyme, and thus useful in the treatment of inflammatory, respiratory and allergic diseases and conditions. Nothing that is disclosed in the above-mentioned applications would teach the person of ordinary skill in the pertinent art the novel compounds of the present invention or their unexpectedly high level of inhibitory activity for the PDE4 isozyme. Reference is also made to copending application Ser. No. 09/345,185 filed Jun. 30, 1999 (Attorney Docket No. PC10096A); claiming priority from application Ser. No. 60/105,120 filed Oct. 21, 1998 (Attorney Docket No. PC10096), which discloses compounds and processes for preparing N-substituted nicotinamide derivatives. However, the disclosed compounds and processes are not the same as those of the present invention. Reference is further made to copending applications filed of even date with the instant application, Attorney Docket Nos. PC10523; PC10546; PC10657; PC10690; and PC10691, which involve other classes of nicotinamide derivatives useful as selective inhibitors of the PDE4 isozyme.

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

- **RAR selective retinoid agonists**

  Inventor(s): Belloni, Paula Nanette; (Half Moon Bay, CA), Jolidon, Synese; (Blauen, CH), Klaus, Michael; (Weil am Rhein, DE), Lapierre, Jean-Marc; (Mountain View, CA)

  Correspondence: HOFFMANN-LA ROCHE INC.; PATENT LAW DEPARTMENT; 340 KINGSLAND STREET; NUTLEY; NJ; 07110

  Patent Application Number: 20020026060

  Date filed: April 23, 2001

  Abstract: New compounds containing bicyclic fused rings, one of which being a phenyl moiety connected by an aliphatic chain to a cycloalkyl or aryl moiety, and pharmaceutically active salts thereof are useful as RAR selective retinoid agonists. Furthermore, such retinoic acid receptor agonists, particularly retinoic acid receptor.gamma. (RAR.gamma.) selective agonists, are useful for the treatment of **emphysema** and associated pulmonary diseases, as well as for the therapy and prophylaxis of dermatological disorders, for the therapy and prophylaxis of malignant and premalignant epithelial lesions, tumors and precancerous changes of the mucous membrane in the mouth, tongue, larynx, esophagus, bladder, cervix and colon.

  Excerpt(s): This invention relates to new RAR selective retinoid agonists and to the use of such retinoic acid receptor agonists, particularly retinoic acid receptor.gamma. (RAR.gamma.) selective agonists for the treatment of **emphysema.** Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality, ranking third and fourth as the leading cause of death in the European Union and North America respectively. COPD is characterized by reduced maximum expiratory flow, which does not change over several months and which persists for 2 or more consecutive years. Patients with the most severe form of COPD generally present with a significant degree of **emphysema. Emphysema** is defined anatomically by permanent airspace enlargement distal to the terminal bronchioles. It is characterized by gradual loss of lung recoil, alveolar destruction, decreased alveolar surface area and gas exchange, leading to a reduced FEV1. These two features, impaired gas exchange and reduction in expiratory flow, are characteristic physiological abnormalities from which patients with **emphysema** suffer. The main symptom of patients with severe **emphysema** is shortness of breath during minimal physical activity. The most common cause of **emphysema** is cigarette smoking although other potential environmental toxins may also contribute. These various insulting agents activate destructive processes in the lung including release of active proteases and free radical oxidants in excess of protective mechanisms. The imbalance in protease/anti-protease levels leads to destruction of the elastin matrix, loss of elastic recoil, tissue damage and continuous decline in lung function. Removing the injurious agents (i.e. quit smoking) slows the rate of damage, however, the damaged alveolar structures do not repair and lung function is not regained.

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

- **Respiratory timing and lung deflation device**

  Inventor(s): Hillsman, Deane; (Sacramento, CA)

  Correspondence: Deane Hillsman; 870 EL Chorro Way; Sacramento; CA; 95864-5244; US

  Patent Application Number: 20030065272

  Date filed: September 28, 2001

Abstract: A portable respiratory prompting device using simple visual and/or auditory means to indicate the onset of inspiration and expiration to prompt a subject into more desirable breathing patterns. Inspiration and expiration are indicated by LED's and simple high and low pitched "beep" sounds. The device is particularly suited for activating previously learned breathing patterns from visual biofeedback training. Optionally patients with **Emphysema** or Asthma may activate an button producing a prolonged expiratory phase to further lung deflation. It is also suited to prompt patients with Hyperventilation Syndrome attacks to slower breathing, and breathing control of subjects in stressful environments such as aircraft pilots or underwater divers, wherein an optional waterproof model is available. It may control breathing in a variety of applications such as pregnant subjects doing Lamaze breathing exercises and athletes in training. It may also be incorporated into clock mechanisms for day and night prompting.

Excerpt(s): This invention relates to improved methods and apparatus to prompt patients with lung disease, and other subjects, into more physiologically appropriate breathing patterns by simple visual and auditory biofeedback means. Hillsman incorporates by reference his U.S. Pat. No. 3,991,304 which describes a sophisticated and complex visual biofeedback device suitable only for medical professional use. This present invention extends that concept into a simple portable device suitable for use under field operational conditions, with both visual and auditory biofeedback means suitable for individual subject use in a lower technical environment. A wide variety of timing metronomes of both mechanical and electrical design have been well known in the music industry for many years. Almost all have been simple devices designed to give an auditory signal of equal periodicity and permitting only an overall rate adjustment. More modern electronic music metronome devices permit a wide spectrum of timing signals suitable for music timing and rhythm coordination needs, and some with visual prompting. This present invention relates to a timing device unique for medical needs wherein the overall rate and the relative timing of inspiration and expiration are adjustable, in essence therefore an "asynchronous metronome" specific to medical respiratory needs. In the course of using Hillsman's advanced visual biofeedback training device, U.S. Pat. No. 3,991,304 it was discovered that native breathing patterns in diseased **emphysema** patients could be altered and that these altered breathing patterns were retained in part (Reference: A Biofeedback Method To Alter Breathing Patterns In COPD; Hillsman, D. and Lillington, G. A.; Third International Conference on Pulmonary Rehabilitation and Mechanical Ventilation; Mar. 12, 1991--Reference: A Visual Biofeedback Method To Define And Teach Breathing Patterns, and, Clinical Experience With A Visual Biofeedback Method In COPD Rehabilitation; Hillsman, D.; International Society for the Advancement of Respiratory Psychophysiology; Second Annual Meeting, Oct. 9, 1995; Biological Psychology, Vol. 43, Issue 3, Jun. 28, 1996, pages 261 and 243-244.) In some unknown manner it is apparent these learned breathing patterns are being imprinted in the patient's subconscious, and recalled and used with a variable degree of accuracy. Though it is usually easy to get patients to follow breathing pattern analogs using the sophisticated visual device, the problem of proper breathing patterns in the home environment remained. Furthermore, many patients would revert to their previous inefficient native breathing patterns under conditions of stress or with the passage of time. It was discovered with the patient blinded, a simple auditory signal to breathe in and out at the appropriate points in the breathing cycle was highly effective in prompting patients into an accurate reproduction of the breathing waveform analog. Thus the concept of the instant invention was created, to activate these learned breathing patterns in a more reliable and accurate manner by means of an auditory "beep" (high pitched) and the beginning of inspiration

and another "beep" (low pitched) at the beginning of expiration. Further, it was considered desirable to use the familiar and soothing "tick/tock" sound of a grandfather clock as the auditory prompt as the preferred embodiment, though the concept could also be implemented with a variety of brief or continuous individual sounds or musical sounds or breath sounds of inspiration and expiration.

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

- **Retinoid compounds (I)**

  Inventor(s): Lapierre, Jean-Marc; (Mountain View, CA), Rotstein, David Mark; (Sunnyvale, CA), Sjogren, Eric Brian; (Mountain View, CA)

  Correspondence: ROCHE BIOSCIENCE; 3401 HILLVIEW AVENUE; INTELLECTUAL PROPERTY LAW DEPT., MS A2-250; PALO ALTO; CA; 94304-9819; US

  Patent Application Number: 20020082265

  Date filed: October 1, 2001

  Abstract: The current invention provide novel retinoid compounds and methods for their synthesis, methods of treating or preventing **emphysema,** cancer and dermatological disorders and pharmaceutical compositions suitable for the treatment or prevention of **emphysema,** cancer and dermatological disorders.

  Excerpt(s): This application claims the benefit of priority of U.S. Provisional Patent Application Serial No. 60/237,459 filed Oct. 2, 2000, which is incorporated herein by reference in its entirety. The invention relates to novel retinoid compounds and methods of synthesis thereof. The invention also relates to methods of using these novel retinoid compounds and pharmaceutical compositions thereof. The retinoids are structural analogues of vitamin A and include both natural and synthetic compounds. Retinoid compounds such as all trans retinoic acid ("ATRA"), 9-cis-retinoic acid, trans 3-4 didehydroretinoic acid, 4-oxo retinoic acid, 13-cis-retinoic acid and retinol are pleiotrophic regulatory compounds that influence a large number of inflammatory, immune and structural cells.

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

- **Surfactant protein D for the prevention and diagnosis of pulmonary emphysema**

  Inventor(s): Whitsett M.D., Jeffrey A.; (Cinncinnati, OH)

  Correspondence: KNOBBE MARTENS OLSON & BEAR LLP; 2040 MAIN STREET; FOURTEENTH FLOOR; IRVINE; CA; 92614; US

  Patent Application Number: 20030172389

  Date filed: April 26, 2000

  Abstract: Surfactant protein D (SP-D) is a 43-kDa member of the collectin family of collagenous lectin domain-containing proteins that is expressed in epithelial cells of the lung. The SP-D gene was targeted by homologous recombination in embryonic stem cells that were used to produce SP-D (-/-) mice. The SP-D (-/-) deficiency caused inflammation, increased oxidant production by isolated alveolar macrophages, abnormal surfactant structure and levels, and decreased SP-A expression. Therefore, disclosed is the SP-D (-/-) mouse as an excellent model for **emphysema.** Also included are models for testing **emphysema** therapies in the mouse model, methods for using SP-

D protein or DNA as a treatment for **emphysema** and pulmonary infections, and diagnosis.

Excerpt(s): This application is a Continuation in Part of PCT/US99/24675, filed Oct. 20, 1999 which claims priority under 35 U.S.C. 119(e) of U.S. Provisional application 60/104941, filing date Oct. 20, 1998. The present invention relates generally to the field of biologically active proteins. More specifically the present invention relates to SP-D proteins involved in pulmonary surfactant homeostasis and structure, and alveolar structure in the lungs and SP-D (-/-) null mice. Pulmonary surfactant is essential for normal lung mechanics and gas exchange in the lung. Pulmonary surfactant is produced by type II epithelial cells and is made up of a phospholipid component which confers the ability of surfactant to lower surface tension in the lung. In addition, there are proteins associated with the surfactant called collectins which are collagenous, lectin domain-containing polypeptides. Two of these, designated surfactant protein A (SP-A) and surfactant protein D (SP-D), are likely involved in surfactant structure and function and host defense. Both quantitative and qualitative deficiencies in pulmonary surfactant are associated with neonatal respiratory distress, adult respiratory distress syndrome, congenital deficiencies of surfactant protein B, and allergic asthma. In addition, deficiency in pulmonary surfactant may contribute to the increased susceptibility of some individuals to microbial challenge, especially in the setting of inadequate or impaired specific immunity. These disorders as well as some disorders associated with increased risk of pneumonia (cystic fibrosis, asthma, prematurity, chronic bronchitis, diffuse alveolar damage) may also be associated with acquired defects or deficiency in collectin function. Alveolar surfactant pools are regulated at multiple levels including intracellular synthesis, secretion, re-uptake and degradation of these components by alveolar macrophages. The synthesis and clearance of surfactant phospholipids and proteins is further influenced by developmental, mechanical, and humoral stimuli that serve to maintain steady-state surfactant concentrations after birth.

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

- **THERAPEUTICALLY ACTIVE COMPOUNDS BASED ON INDAZOLE BIOISOSTERE REPLACEMENT OF CATECHOL IN PDE4 INHIBITORS**

  Inventor(s): MARFAT, ANTHONY; (MYSTIC, CT)

  Correspondence: PAUL H GINSBURG; PFIZER INC; 235 EAST 42ND STREET; 20TH FLOOR; NEW YORK; NY; 10017-5755; US

  Patent Application Number: 20020058687

  Date filed: September 20, 1999

  Abstract: Therapeutically active compositions of matter are described which are useful for treating or preventing diseases and conditions comprising inflammatory diseases including joint inflammation, Crohn's disease, and inflammatory bowel disease; respiratory diseases such as chronic obstructive pulmonary disease (COPD) including asthma, chronic bronchitis, and pulmonary **emphysema;** infectious diseases including endotoxic shock and toxic shock syndrome; immune diseases including systemic lupus erythematosis and psoriasis; and other diseases including bone resorption diseases and reperfusion injury; wherein said composition of matter comprises a compound which is an inhibitor of phosphodiesterase isozyme 4 (PDE4) and wherein an indazole is one essential component of said compound's overall chemical structure, and wherein said indazole constitutes a bioisosteric replacement of a catechol component or functional derivative thereof in a known compound having the same said therapeutic activity and

the same remaining said components of its overall chemical structure. Included are compounds of Formula (IA) or (IB), wherein R.sup.2.sub.a and R.sup.2.sub.b are independently selected from the group consisting essentially of hydrogen and hereinafter recited substituents, provided that one, but not both of R.sup.2.sub.a and R.sup.2.sub.b must be independently selected as hydrogen, wherein said substituents comprise moieties including the following: (IC), (ID), (IE), (IF), (ILA), (ILB), (IIC), (IID), (IIE), (IIF), (IIG), (IIH), (III), (IIIA), (IIIB), (IIIC), (IIID), (IIIE), (IIIF), (IIIG), (IIIH), (IIII), (IIIJ), (IIIK), (IIIL), (IIIM), (IIIN), (IIIO), (IIIP), (IIIR), (IIIS), (IIIT), (IV), (VA), (VB), (VC), (VD), (VE.sub.a), (VE), (VF), (VG), (VH), (VI), (VJ), (VK), (VL), (VM). 1

Excerpt(s): The present invention is in the field of compositions of matter, and pharmaceutical compositions and methods of treatment utilizing one or more of said compositions of matter as the active ingredient and the active agent with respect thereto, wherein said composition of matter comprises an indazole as an essential feature of its overall chemical structure, said indazole constituting a bioisosteric replacement of a catechol or functional derivative thereof. The catechol-containing as well as the indazole-based compositions of matter have biological activity as selective inhibitors of phosphodiesterase (PDE) type IV and the production of tumor necrosis factor (TNF), and as such are useful in the treatment of asthma, chronic obstructive pulmonary disease (COPD), psoriasis, allergic rhinitis, dermatitis, Crohn's disease, arthritis, and other inflammatory diseases, AIDS, septic shock and other diseases involving the production of TNF. This invention also relates to a method of using such compounds in the treatment of the foregoing diseases in mammals, especially humans, and to pharmaceutical compositions containing such compounds. Since the recognition that cyclic adenosine phosphate (AMP) is an intracellular second messenger, E. W. Sutherland, and T. W. Rall, Pharmacol. Rev., 12, 265, (1960), inhibition of the phosphodiesterases has been a target for modulation and, accordingly, therapeutic intervention in a range of disease processes. More recently, distinct classes of PDE have been recognized, J. A. Beavo et al., TiPS, 11, 150, (1990), and their selective inhibition has led to improved drug therapy, C. D. Nicholson, M. S. Hahid, TiPS, 12, 19, (1991). More particularly, it has been recognized that inhibition of PDE type IV can lead to inhibition of inflammatory mediator release, M. W. Verghese et al., J. Mol. Cell Cardiol., 12 (Suppl. II), S 61, (1989) and airway smooth muscle relaxation (T. J. Torphy in "Directions for New Anti-Asthma Drugs," eds S. R. O'Donnell and C. G. A. Persson, 1988, 37 Birkhauser-Verlag). Thus, compounds that inhibit PDE type IV, but which have poor activity against other PDE types, would inhibit the release of inflammatory mediators and relax airway smooth muscle without causing cardiovascular effects or antiplatelet effects.

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

- **Use of inhaled retinoids in the treatment of lung diseases**

  Inventor(s): Tong, William P.; (Flushing, NY), Warrell, Raymond P. JR.; (Westfield, NJ)

  Correspondence: OPPEDAHL AND LARSON LLP; P O BOX 5068; DILLON; CO; 80435-5068; US

  Patent Application Number: 20020035152

  Date filed: May 11, 2001

  Abstract: Administration of retinoids by inhalation is used to overcome the chronic toxicity problems presented by systemic administration and to make retinoid therapy available as an option for the treatment of fibrotic lung disease, **emphysema,** and the

prevention and treatment of epithelial cancers of the respiratory tract, especially those that are associated with tobacco use. Retinoids are administered by inhalation to the respiratory tract of the individual as an air-borne composition with a metered dose aerosol-producing inhaler, in which the retinoid is dissolved in a combination of a pharmaceutically acceptable chlorofluorocarbon propellant and an alkylamine solubilizing agent.

Excerpt(s): This application is a continuation-in-part of U.S. patent application Ser. No. 09/171,478 filed Dec. 29, 1998, which is a national phase of International Application Ser. No. PCT/US97/05409 which claims the benefit of priority from U.S. Provisional App. Ser. No. 60/016,246 filed Apr. 19, 1996. Unfortunately, while retinoids have been shown to provide beneficial effects in the prevention of at least some types of cancer, the therapeutic regiment requires chronic administration. Under these circumstances, substantial systemic toxicity may result, including hepatic dysfunction, skeletal malformations, mucositis, hyperlipidemia, hypertriglyceridemia (possibly leading to accelerated atherosclerosis and pancreatitis), hypercalcemia, birth defects, and skin, liver and central nervous system toxicity. This toxicity has limited the utility of retinoids as therapeutic agents in the prevention of cancer and in the treatment of lung diseases. Several potential strategies for mitigating the toxicity of retinoids have been considered, including "drug holidays", reductions in dosage, and development of naturally occurring or synthetic ligands that bind specific nuclear retinoid receptors. Lotan, R., FASEB J 10: 1031 (1996). However, none of these strategies has yielded a substantial increase in therapeutic index.

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

Keeping Current

In order to stay informed about patents and patent applications dealing with emphysema, you can access the U.S. Patent Office archive via the Internet at the following Web address: **http://www.uspto.gov/patft/index.html**. You will see two broad options: (1) Issued Patent, and (2) Published Applications. To see a list of issued patents, perform the following steps: Under "Issued Patents," click "Quick Search." Then, type "emphysema" (or synonyms) into the "Term 1" box. After clicking on the search button, scroll down to see the various patents which have been granted to date on emphysema.

You can also use this procedure to view pending patent applications concerning emphysema. 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 EMPHYSEMA

Overview

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

- **Living a Healthy Life With Chronic Conditions: Self-Management of Heart Disease, Arthritis, Stroke, Diabetes, Asthma, Bronchitis, Emphysema and Others**

  Source: Palo Alto, CA: Bull Publishing Company. 1994. 296 p.

  Contact: Available from Bull Publishing Company. P.O. Box 208, Palo Alto, CA 94302-0208. (800) 676-2855 or (415) 322-2855. Fax (415) 327-3300. E-mail: BullPublishing@msn.com. PRICE: $14.95. ISBN: 0923521283.

  Summary: This book is a complete self-management guide for people with chronic diseases. The authors focus on day-to-day living skills, in the context of the specific chronic diseases, including heart disease, arthritis, stroke, diabetes, asthma, bronchitis, and emphysema. General topics include the psychological aspects to self-management; finding resources; smoking and quitting; understanding common symptoms; using one's mind to manage symptoms; exercising for fun and fitness; exercising for flexibility and strength; exercising for endurance; exercising tips for people with specific chronic

diseases; the importance of communication; durable powers of attorney for health care; eating well; and managing medications. The chapter on diabetes covers diabetes and its causes; maintaining an appropriate blood glucose level; symptoms of hyperglycemia and hypoglycemia; dietary management; exercise; insulin injections; oral medications; emotions; self-monitoring of blood glucose and urine; the complications of diabetes; and diabetes resources. Each chapter includes limited references and a subject index concludes the volume.

Book Summaries: Online Booksellers

Commercial Internet-based booksellers, such as Amazon.com and Barnes&Noble.com, offer summaries which have been supplied by each title's publisher. Some summaries also include customer reviews. Your local bookseller may have access to in-house and commercial databases that index all published books (e.g. Books in Print®). **IMPORTANT NOTE:** Online booksellers typically produce search results for medical and non-medical books. When searching for "emphysema" at online booksellers' Web sites, you may discover non-medical books that use the generic term "emphysema" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "emphysema" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **624 Supplement: Pulmonary Emphysema - the Rationale for Therapeutic Intervention (Annals of the New York Academy of Sciences)** by Allen B. Cohen (Editor); ISBN: 0897667239; http://www.amazon.com/exec/obidos/ASIN/0897667239/icongroupinterna
- **A Treatment Manual for Patients With Pulmonary Emphysema** by Alvan Leroy Barach; ISBN: 0808900307; http://www.amazon.com/exec/obidos/ASIN/0808900307/icongroupinterna
- **Asthma, Emphysema, and Chronic Bronchitis: Expert Drug Therapy Video Series (Expert Drug Therapy Video Series)** by Blanchard, et al (2001); ISBN: 193013813X; http://www.amazon.com/exec/obidos/ASIN/193013813X/icongroupinterna
- **Battle to breathe; what you need to know about emphysema** by Louis J. Klingbeil; ISBN: 0812700597; http://www.amazon.com/exec/obidos/ASIN/0812700597/icongroupinterna
- **Biochemistry of Pulmonary Emphysema (Current Topics in Rehabiliation)** by C. Grassi, et al; ISBN: 0381197751; http://www.amazon.com/exec/obidos/ASIN/0381197751/icongroupinterna
- **Biochemistry, Pathology and Genetics of Pulmonary Emphysema: Proceedings of a Meeting on Emphysema Held at Porto Conte, April 27-30,1980** by G.L. Scarpa (Editor), Jean Bignon (1981); ISBN: 0080273793; http://www.amazon.com/exec/obidos/ASIN/0080273793/icongroupinterna
- **Breathing Free : The Revolutionary 5-Day Program to Heal Asthma, Emphysema, Bronchitis,and Other Respiratory Ailments** by Teresa Hale (Author) (2000); ISBN: 0609806343; http://www.amazon.com/exec/obidos/ASIN/0609806343/icongroupinterna
- **Chronic Bronchitis and Emphysema: Report by the Industrial Injuries Advisory Council in Accordance with Section 171 of the Social Security Administration Act 1992 Reviewing the Prescription of Chronic Bronchitis and Emphysema for**

Underground Coal Workers (Cm: 3240) by J.M. Harrington (1996); ISBN: 0101324022; http://www.amazon.com/exec/obidos/ASIN/0101324022/icongroupinterna

- **Chronic Obstructive Pulmonary Disease: Practical, Medical, and Spiritual Guidelines for Daily Living With Emphysema, Chronic Bronchitis, and Combination Diagnosis** by Mark Jenkins; ISBN: 1568383509; http://www.amazon.com/exec/obidos/ASIN/1568383509/icongroupinterna
- **Coping With Bronchitis and Emphysema** by Tom Smith (1994); ISBN: 0859697096; http://www.amazon.com/exec/obidos/ASIN/0859697096/icongroupinterna
- **Cor Pulmonale in Chronic Bronchitis and Emphysema** by M. L. Murphy; ISBN: 0879932260; http://www.amazon.com/exec/obidos/ASIN/0879932260/icongroupinterna
- **Courage and Information for Life with Chronic Obstructive Pulmonary Disease: The Handbook for Patients, Families and Care Givers Managing COPD, Emphysema, Bronchitis** by Rick Carter, et al (2001); ISBN: 1882431073; http://www.amazon.com/exec/obidos/ASIN/1882431073/icongroupinterna
- **Early detection of chronic bronchitis and pulmonary emphysema** by Dan C. Stanescu; ISBN: 0397581890; http://www.amazon.com/exec/obidos/ASIN/0397581890/icongroupinterna
- **Emphysema (A Love Story)** by Janet Munsil; ISBN: 0921833717; http://www.amazon.com/exec/obidos/ASIN/0921833717/icongroupinterna
- **Emphysema and Chronic Bronchitis.** by Stanton. Belinkoff; ISBN: 0316088005; http://www.amazon.com/exec/obidos/ASIN/0316088005/icongroupinterna
- **Emphysema and Common Sense,** by Spencer H. Robley; ISBN: 0132747952; http://www.amazon.com/exec/obidos/ASIN/0132747952/icongroupinterna
- **Emphysema: A Doctor's Advice for Patients and Their Families,** by Fred A. Obley; ISBN: 0807021865; http://www.amazon.com/exec/obidos/ASIN/0807021865/icongroupinterna
- **Enjoying Life With Emphysema** by Thomas L. Petty, et al; ISBN: 0812111028; http://www.amazon.com/exec/obidos/ASIN/0812111028/icongroupinterna
- **Enjoying Life With Emphysema**; ISBN: 0812109139; http://www.amazon.com/exec/obidos/ASIN/0812109139/icongroupinterna
- **Fact/Book on Sinusitis, Bronchitis and Emphysema and Their Natural Treatment** by Clifford Quick; ISBN: 9995344300; http://www.amazon.com/exec/obidos/ASIN/9995344300/icongroupinterna
- **For those who live and breathe with emphysema and chronic bronchitis** by Thomas L. Petty (Author), Louise M. Nett (Author); ISBN: B00005VY6A; http://www.amazon.com/exec/obidos/ASIN/B00005VY6A/icongroupinterna
- **For Those Who Live and Breathe: A Manual for Patients With Emphysema and Chronic Bronchitis** by Thomas L. Petty; ISBN: 0398023808; http://www.amazon.com/exec/obidos/ASIN/0398023808/icongroupinterna
- **Living a Healthy Life with Chronic Conditions: Self-Management of Heart Disease, Arthritis, Diabetes, Asthma, Bronchitis, Emphysema & Others** by Kate Lorig (Editor), et al; ISBN: 0923521534; http://www.amazon.com/exec/obidos/ASIN/0923521534/icongroupinterna

- **Living Well With Chronic Asthma, Bronchitis, and Emphysema** by Myra B. Shayevitz, Berton R. Shayevitz (Contributor); ISBN: 0890434166; http://www.amazon.com/exec/obidos/ASIN/0890434166/icongroupinterna
- **Living Well With Emphysema and Bronchitis: A Handbook for Everyone With Chronic Obstructive Pulmonary Disease** by Myra, Md. Shayevitz, Berton R. Shayevitz; ISBN: 0385194382; http://www.amazon.com/exec/obidos/ASIN/0385194382/icongroupinterna
- **Living With Your Bronchitis and Emphysema** by Theodore Berland; ISBN: 0312491409; http://www.amazon.com/exec/obidos/ASIN/0312491409/icongroupinterna
- **Lung Volume Reduction Surgery for Emphysema (Lung Biology in Health and Disease, 184)** by Henry E. Fessler (Editor), et al (2003); ISBN: 0824708970; http://www.amazon.com/exec/obidos/ASIN/0824708970/icongroupinterna
- **Molecular Biology of the Lung:Emphysema and Inflation (Respiratory Pharmacology and Pharmacotheraphy , Vol 1)** by Robert A. Stockley (1999); ISBN: 3764358572; http://www.amazon.com/exec/obidos/ASIN/3764358572/icongroupinterna
- **Natural Hist Chronic Bronchitis Emphysema** by C. Fletcher, et al (1985); ISBN: 0192611194; http://www.amazon.com/exec/obidos/ASIN/0192611194/icongroupinterna
- **Nature cure for bronchitis and emphysema** by Clifford Quick; ISBN: 0852690002; http://www.amazon.com/exec/obidos/ASIN/0852690002/icongroupinterna
- **None Need Suffer from Asthma: Nor in All Probability Develop Emphysema** by Jacob John Robbins; ISBN: 0682402249; http://www.amazon.com/exec/obidos/ASIN/0682402249/icongroupinterna
- **Pathology of chronic bronchitis and emphysema** by Brian Edyvean Heard; ISBN: 0700014195; http://www.amazon.com/exec/obidos/ASIN/0700014195/icongroupinterna
- **Pathology of Idsruptive Pulmonary Emphysema** by Anderson; ISBN: 0398035288; http://www.amazon.com/exec/obidos/ASIN/0398035288/icongroupinterna
- **Pathophysiological Basis of the Effects of Lung Volume Reduction Surgery: Insights from Its Application in an Animal Model of Emphysema (Acta Biomedica Lovaniensia, 264)** by Eric Marchand (2002); ISBN: 9058672352; http://www.amazon.com/exec/obidos/ASIN/9058672352/icongroupinterna
- **Perspectives of Antioxidant Treatment of Emphysema With N-Acetyloysteine** by V. Cichetti (Editor), et al (1986); ISBN: 3805545142; http://www.amazon.com/exec/obidos/ASIN/3805545142/icongroupinterna
- **Pulmonary emphysema : proceedings of the International Symposium on Pathophysiology and Diagnostic Methods in Incipient Pulmonary Emphysema, Porto Conte, Alghero, April 6-9, 1974**; ISBN: 3805522738; http://www.amazon.com/exec/obidos/ASIN/3805522738/icongroupinterna
- **Pulmonary Emphysema and Proteolysis 1986** by Joseph C. Taylor, Charles Mittman (Editor); ISBN: 0126845700; http://www.amazon.com/exec/obidos/ASIN/0126845700/icongroupinterna
- **Pulmonary emphysema and related lung diseases** by Theodore Rodman; ISBN: 0801641403; http://www.amazon.com/exec/obidos/ASIN/0801641403/icongroupinterna

- **Pulmonary Emphysema: The Rationale for Therapeutic Intervention (Annals of the New York Academy of Sciences, Vol. 624)** by George Weinbaum, et al; ISBN: 0897666593; http://www.amazon.com/exec/obidos/ASIN/0897666593/icongroupinterna
- **Pulmonary Emphysema: The Rationale for Therapeutic Intervention: Proceedings of a Follow-Up Workshop on Treating the Underlying Causes of Emphysema** by Allen B. Cohen (1991); ISBN: 0897667247; http://www.amazon.com/exec/obidos/ASIN/0897667247/icongroupinterna
- **The Chronic Bronchitis and Emphysema Handbook** by François Haas (Author), Sheila Sperber Haas (Author); ISBN: 047123995X; http://www.amazon.com/exec/obidos/ASIN/047123995X/icongroupinterna
- **The no-drug approach to conquering asthma and controlling emphysema** by George E. Berkley; ISBN: 0915962349; http://www.amazon.com/exec/obidos/ASIN/0915962349/icongroupinterna
- **The Quiet Killer: Emphysema/Chronic Obstructive Pulmonary Disease** by Hannah L. Hedrick (Editor), et al (2002); ISBN: 0810841738; http://www.amazon.com/exec/obidos/ASIN/0810841738/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 "emphysema" (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]

- **A special report on emphysema.** Author: National Institute of Allergy and Infectious Diseases (U.S.); Year: 1967; [Bethesda? Md. 1967]
- **A treatment manual for patients with pulmonary emphysema.** Author: Barach, Alvan L. (Alvan Leroy),; Year: 1961; New York, Grune; Stratton [c1969]
- **Cardiomyopathy, pulmonary emphysema; proceedings of the tenth conference of the International Society of Geographical Pathology, Jerusalem, September 1-4, 1969. Published on behalf of the directing committee of the Society by Dr. J. R. Rüttner.** Author: International Society of Geographical Pathology.; Year: 1968; Basel, New York, Karger, 1970
- **Chronic bronchitis and pulmonary emphysema rehabilitation manual.** Author: Chronic Respiratory Diseases Control Program (National Center for Chronic Disease Control); Year: 1967; Arlington, Va. [1967?]

---

[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**.

- **Cor pulmonale in emphysema: mechanisms and pathology, by Donald Heath, Douglas Brewer, and Peter Hicken.** Author: Heath, Donald.; Year: 1963; Springfield, Ill., Thomas [c1968]
- **Emphysema and common sense.** Author: Robley, Spencer H.; Year: 1968; West Nyack, Parker [c1968]
- **Emphysema, the growing problem of breathlessness.** Author: Saltman, Jules.; Year: 1965; [New York, Public Affairs Committee, c1972]
- **Emphysema; a doctor's advice for patients and their families.** Author: Obley, Fred A.,; Year: 1968; Boston, Beacon Press [c1970]; ISBN: 807021865
- **Emphysema; the battle to breathe.** Author: Carey, Frank E.; Year: 1968; Arlington, Va., National Center for Chronic Disease Control, Chronic Respiratory Diseases Control Program; [for sale by the Supt. of Docs., U. S. Govt. Print. Off., Washington, 1967]
- **Essentials of living with pulmonary emphysema; a guide for patients and their families.** Author: Haas, Albert,; Year: 1962; New York, Institute of Physical Medicine and Rehabilitation, New York University Medical Center [1963]
- **For those who live and breathe with emphysema and chronic bronchitis, by Thomas L. Petty and Louise M. Nett.** Author: Petty, Thomas L.,; Year: 1969; Springfield, Ill., Thomas [c1967]
- **Functional exploration of the respiratory and cardiovascular system in asthma, emphysema and related disorders; proceedings of the small meeting, Barcelona, 1960.** Author: European Academy of Allergy.; Year: 1966; Leiden, Kroese, 1961
- **If you have emphysema or chronic bronchitis.** Author: Chronic Respiratory Diseases Control Program (National Center for Chronic Disease Control); Year: 1967; [Arlington, Va., For sale by the Supt. of Docs., U. S. Govt. Print. Off., Washington, 1968]
- **Living with your bronchitis and emphysema [by] Theodore Berland and Gordon L. Snider.** Author: Berland, Theodore,; Year: 1968; New York, St. Martin's Press [1972]
- **Nature cure for bronchitis and emphysema.** Author: Quick, Clifford.; Year: 1965; Croydon [Eng.] Health for All Pub. Co. [1968]; ISBN: 852690002
- **Pathology of chronic bronchitis and emphysema.** Author: Heard, Brian Edyvean.; Year: 1968; Baltimore, Williams; Wilkins, 1969; ISBN: 700014195
- **Prevalence of respiratory symptoms, chronic bronchitis and pulmonary emphysema in a Finnish rural population; field survey of age group 40-64 in the Harjavalta area.** Author: Huhti, Esko.; Year: 1967; Copenhagen, Munksgaard, 1965
- **Pulmonary emphysema and proteolysis, edited by Charles Mittman.** Author: Mittman, Charles.; Year: 1960; New York, Academic Press, 1972; ISBN: 0125007507
- **Pulmonary emphysema and related lung diseases [by] Theodore Rodman [and] Francis H. Sterling.** Author: Rodman, Theodore.; Year: 1965; St. Louis, Mosby, 1969; ISBN: 801641403
- **The pathology of emphysema.** Author: Reid, Lynne M.; Year: 1960; Chicago, Year Book Medical Publishers, 1967
- **You and your emphysema.** Author: Obley, Fred A.,; Year: 1964; Philadelphia, Toronto, Lippincott [c1968]

Chapters on Emphysema

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

- **Pulmonary Disease**

  Source: in Little, J.W., et al. Dental Management of the Medically Compromised Patient. 5th ed. St. Louis, MO: Mosby, Inc. 1997. p. 241-259.

  Contact: Available from Harcourt Health Sciences. 11830 Westline Industrial Drive, St. Louis, MO 63146. (800) 325-4177. Fax (800) 874-6418. Website: www.harcourthealth.com. PRICE: $48.00 plus shipping and handling. ISBN: 0815156340.

  Summary: A working knowledge of the multitude of compromised health states is essential for dental professionals, as the majority of medically compromised patients need or want oral health care. This chapter on pulmonary (lung) disease is from a text that provides the dental practitioner with an up to date reference work describing the dental management of patients with selected medical problems. The authors focus on some of the more commonly encountered pulmonary conditions, including chronic obstructive pulmonary disease (COPD, including chronic bronchitis and emphysema), asthma, and tuberculosis. The authors discuss incidence and prevalence of each condition, its etiology (including genetic and lifestyle causes), pathophysiology and complications, signs and symptoms (clinical presentation and laboratory findings), the medical management of patients with pulmonary diseases, and the dental management of this population. 7 figures. 8 tables. 45 references.

- **Managing the Patient with Severe Respiratory Problems**

  Source: in Homestead Schools, Inc. Medically Compromised Patient. Torrance, CA: Homestead Schools, Inc. 1999. p. 19-39.

  Contact: Available from Homestead Schools, Inc. 23844 Hawthorne Boulevard, Suite 200, Torrance, CA 90505. (310) 791-9975. Fax (310) 791-0135. E-mail: Education@homesteadschools.com. Website: www.homesteadschools.com. PRICE: $24.00 plus shipping and handling.

  Summary: The dental management of patients with severe respiratory problems continues to be a significant challenge to the dental health care practitioner. Chronic obstructive pulmonary diseases, such as chronic bronchitis and **emphysema,** are the fourth leading cause of death in the United States. Asthma has increased in prevalence during the past 20 years, and the rate of death from this chronic inflammatory diseases of the airways has also risen despite recent advances in medical treatments. This book chapter reviews the pathophysiology and medical treatment modalities for these chronic pulmonary diseases, as well as discuss the recognition and management of dental patients with these diseases and provide an understanding on how to avoid precipitating factors that could initiate an acute episode in the dental care setting. The author concludes that patients with severe respiratory problems can receive safe and

appropriate care when the dental team has conducted a proper risk assessment and tailored the necessary dental treatment to each individual patient's needs and tolerance. Preparation is vital to the prevention of a medical emergency arising from dental treatment in patients who are compromised by serious health conditions. This chapter is from a continuing education manual on management of the medically compromised patient. 2 tables. 41 references.

- **Acquired Disorders Affecting the Teeth**

  Source: in Scully, C., et al. Color Atlas of Orofacial Health and Disease in Children and Adolescents. London, England: Martin Dunitz Ltd. 2002. p.71-103.

  Contact: Available from Martin Dunitz Ltd, The Livery House. 7-9 Pratt Street, London, England NW1 0AE. 4404074822202. Website: www.dunitz.co.uk. Email: info@mdunitz.globalnet.co.uk. PRICE: $125.00 plus shipping and handling. ISBN: 1841841021.

  Summary: This chapter on acquired disorders affecting the teeth is from a full-color atlas that covers the presentation of the common orofacial disorders and a wide range of less common and some rare disorders. The chapter begins with a brief section on common complaints, covering early loss of teeth, variations in tooth eruption times, variations in tooth number, and variations in tooth size, shape, structure, and color. Disorders are then outlined, including abrasion, ankylosis, attrition, dental caries (cavities), periapical abscess, dilacerations, double teeth (connation), enamel cleft, enamel hypoplasia, erosion, eruption cyst and hematoma, external resorption, extrinsic staining, hyperdontia, hyperplastic pulpitis (pulp polyp), hypodontia, impacted teeth, internal resorption (pink spot), intrinsic staining, macrodontia, malocclusion, odontomes, prominent tubercles or cusps, taurodontism, transposition, trauma, child abuse (nonaccidental injury), and surgical **emphysema.** Full-color photographs are accompanied by brief text entries describing each condition and noting diagnostic and management considerations for each. 98 figures. 7 tables.

- **How Vocal Abilities Can Be Limited by Non-Infectious Diseases and Disorders of the Respiratory and Digestive Systems**

  Source: in Thurman, L. and Welch, G., eds. Bodymind and Voice: Foundations of Voice Education, Volumes 1-3. 2nd ed. Collegeville, MN: VoiceCare Network. 2000. p. 546-555.

  Contact: Available from National Center for Voice and Speech (NCVS). Book Sales, 334 Speech and Hearing Center, University of Iowa, Iowa City, IA 52242. Website: www.ncvs.org. PRICE: $75.00 plus shipping and handling. ISBN: 0874141230.

  Summary: This chapter on noninfectious diseases and disorders of the respiratory and digestive systems is from a multi-volume text that brings a biopsychosocial approach to the study of the voice. The authors use the phrase 'bodyminds' to describe the interrelationship of perception, memory, learning, behavior, and health, as they combine to affect all environmental interactions, adaptations, and learning. The books are written for teachers, voice professionals, people who use their voices on an avocational basis, and interested members of the general public. This chapter describes the effects of smoking and other pollutants, sinusitis and rhinitis, laryngitis, bronchitis and other pulmonary (lung) diseases, the effects of outdoor and indoor air pollution, normal and disordered nasal (nose) conditions, asthma, obstructive sleep apnea, **emphysema,** and gastroesophageal reflux disease (GERD, the return of stomach acid to the esophagus and larynx). GERD can result in hoarseness, lowering of the average speaking pitch range, increased effort when singing, and a 'tired voice.' Asthma can affect voice primarily by

decreasing the ability of the respiratory system to inhale and then pressurize the lung air to create sufficient breathflow between the vocal folds. Asthma symptoms can be triggered by inhalation of allergens or pollutant particles of irritant chemicals, infection, cold air, vigorous exercise, acute neuropsychobiological distress, or even vigorous singing. 68 references.

- **Why Do Human Beings Develop Groin Hernias?**

  Source: in Fitzgibbons, R.J.; Greenberg, A.G., eds. Nyhus and Condon's Hernia. Philadelphia, PA: Lippincott Williams and Wilkins. 2002. p.3-8.

  Contact: Available from Lippincott Williams and Wilkins. P.O. Box 1600, Hagerstown, MD 21741. (800) 638-3030 or (301) 223-2300. Fax (301) 223-2365. PRICE: $179.00 plus shipping and handling. ISBN: 0781719623.

  Summary: This introductory chapter is from a lengthy textbook on the surgical management of hernias. In this chapter, the author considers why humans develop groin hernias. Topics include the anatomy of inguinal herniation, the congenital influence on the processus vaginalis, the fascia, metabolic factors, cigarette smoking and proteolysis, metastatic **emphysema,** aneurysm, genetic influences, spontaneous or iatrogenic trauma, physical exertion, and femoral herniation. Appended to the chapter is an editor's comment. The role of a genetically defined biochemical abnormality of fascia in patients with groin hernia is explored and supported by recent research. 23 references.

CHAPTER 8. MULTIMEDIA ON EMPHYSEMA

Overview

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

- **Aging Brain**

  Source: Sacramento, CA: Department of Aging. 1987. (videocassette, 6 handouts and 6 page training manual.).

  Contact: California Department of Aging, Training and Education Section. 1600 K Street, Sacramento, CA 95814. (916) 322-3110. PRICE: $10.00.

  Summary: This tape contains seven training segments designed for administrators and staff working in residential facilities for the aged. It reviews commonly held beliefs about aging that may negatively influence the care given to aging residents and how these myths developed. According to the tape, many believe that aged people are naturally "senile". Aged people can either accept this belief and act accordingly, creating a self-fulfilling prophecy in which they relinquish their independence to those caring for them, or they can rebel against their caregivers. Several studies related to aging are reviewed that suggest that there are only minor differences between the mental capacities of the young and aged. Treatable diseases that can affect the aged person's

mental abilities are described including drug overdoses, malnutrition, dehydration, blood clots, brain tumors, depression, alcoholism, liver failure, kidney failure, drastic environmental changes, thyroid problems, heart failure, infections, diabetes, constipation, and **emphysema.** Organic brain syndromes, incurable diseases that affect mental capability, also are reviewed, including multi-infarct dementia, Pick's disease, Creutzfeldt-Jakob disease, Korsakoff's syndrome, Parkinson's disease, and Alzheimer's disease. Specific attention is given to changes in the brain that occur as the disease progresses, the symptoms, and possible risk factors and causes of the disease. Contact points for the Alzheimer's Association are provided for further information.

- **Basics of Alpha 1-Antitrypsin Liver Disease**

  Source: Washington, DC: Alpha-1 Association. 200x. (videorecording).

  Contact: Available from Alpha-1 Association. 1225 Eye Street NW, Suite 1225, Washington, DC 20005-5918. (800) 521-3025 or (202) 887-1900. Fax: (202) 887-1964. Website: www.alpha1.org. E-mail: info@alpha1.org. PRICE: Contact organization for copies.

  Summary: This videocassette depicts a slide lecture program given by Dr. Jeffrey Teckman at an Alpha-1 Association conference. Dr. Teckman describes the physiology and chemistry of the alpha-antitrypsin system, then the pathophysiology of alpha1-antitrypsin deficiency. Dr. Teckman uses highly technical language, but then defines his terms and uses graphics to explain how the pathophysiology works (not all slides to which he refers are included in this videotape). Dr. Teckman also discusses the complications that are seen with this common, but underdiagnosed, genetic liver disease, including chronic hepatitis (liver inflammation), cirrhosis (scarring of the liver), liver cancer, and **emphysema.** Other topics include the Swedish research study that provided a great deal of basic information about this disease, the genetics, screening, diagnosis, the role of liver biopsy in diagnosis, and treatment options. The program concludes with a section of questions from the lecture audience, along with Dr. Teckman's answers.

- **Diagnosing Alpha 1 Antitrypsin Deficiency**

  Source: Minneapolis, MN: Alpha 1 Association. 199x. (videocassette).

  Contact: Available from Alpha 1 Association. 8120 Penn Avenue, South, Suite 549, Minneapolis, MN 55431-1326. (800) 521-3025 or (612) 703-9979. Fax (612) 703-9977. E-mail: A1NA@alpha1.org. Website: www.alpha1.org. PRICE: $3.00 plus shipping and handling.

  Summary: This videotape program, narrated by Sandra Brandley, the Executive Director of the Alpha 1 National Association, reminds physicians of the symptoms and differential diagnosis of alpha 1 antitrypsin deficiency (A1AD or Alpha 1). The program features Dr. James Stoller, who describes the typical underdiagnosis of A1AD which is typical: the mean time until diagnosis is 7 years (from onset of symptoms) and the mean number of doctors consulted before diagnosis is 3.5. Alpha 1 is a relatively common genetic disorder that affects infants, children, and adults. It is the most common metabolic disorder that causes liver disease in infants and children; the disorder also causes cirrhosis and cancer of the liver in adults. Symptoms of A1AD deficiency in children include prolonged obstructive jaundice, low birth weight, mildly elevated liver enzymes, cholestasis, enlarged liver, abnormal bleeding, feeding difficulties, poor growth (or failure to thrive), and ascites (abnormal accumulation of fluids). In adults, the spectrum of liver disease associated with A1AD deficiency varies from mild to

severe. Symptoms include chronic active hepatitis, cryptogenic cirrhosis (liver scarring of unknown cause), portal hypertension (high blood pressure in the portal vein of the liver), and hepatocellular carcinoma (liver cancer). A rare but telling symptom is panniculitis, a chronic inflammation of subcutaneous fat featuring ulcerated skin lesions on the torso. Dr. Stoller reminds viewers of the indications for A1AD screening: premature onset of moderate to severe chronic obstructive pulmonary disease (COPD) before age 50; predominant basilar **emphysema;** chronic bronchitis with airflow obstruction in a nonsmoker; bronchiectasis (irreversible dilation and destruction of the bronchial walls) without clear risk factors; development of unremitting asthma; family history of A1AD; cirrhosis without apparent risk factors; and family history of panniculitis. The program includes a chart of laboratory values and the risk of development of A1AD, and a series of interviews with patients about the interplay of early diagnosis and good quality of life. The program concludes with the contact information for the Alpha 1 National Association (800-521-3025).

Bibliography: Multimedia on Emphysema

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 emphysema (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 emphysema:

- **Asthma, emphysema, and chronic bronchitis [videorecording]** Source: [presented by] Blanchard & Loeb Publishers, LLC; Year: 2000; Format: Videorecording; Newark, NJ: Blanchard & Loeb Publishers, c2000
- **Asthma, emphysema, and chronic bronchitis [videorecording]** Source: produced by Blanchard & Loeb Publishers; Year: 2001; Format: Videorecording; Glenmoore, PA: Blanchard & Loeb Publishers, c2001
- **Bronchitis and emphysema [slide]** Source: Averill A. Liebow; Year: 1973; Format: Slide; San Diego, Calif.: Liebow: [for sale by Cal-Med Photo, 1973?]
- **Care of the patient with emphysema [filmstrip]** Source: Trainex Corporation; Year: 1971; Format: Filmstrip; Garden Grove, Calif.: Trainex, c1971
- **Chronic bronchitis and emphysema [videorecording]: a treatment update** Source: University of Washington, Department of Medicine; produced in the facilities of Instructional Media Services, University of Washington; Year: 1991; Format: Videorecording; [Seattle, Wash.]: The University, c1991
- **Chronic bronchitis and pulmonary emphysema: the application of physical medicine and rehabilitation, part I [motion picture]** Source: Public Health Service, Division of Chronic Diseases and New York University Medical Center, Institute of Physical Medicine and; Year: 1965; Format: Motion picture; [Washington]: The Service; [Atlanta: for loan by National Medical Audiovisual Center, 1965]
- **Chronic bronchitis and pulmonary emphysema: the application of physical medicine and rehabilitation, part II [motion picture]** Source: Public Health Service, Division of Chronic Diseases and New York University Medical Center, Institute of Physical Medicine and; Year: 1964; Format: Motion picture; [Washington]: The Service, [1964]

- **Diagnostic tests for bronchitis and emphysema [motion picture]** Source: U. S. Department of Health, Education, and Welfare, Public Health Service; Year: 1965; Format: Motion picture; [Washington]: The Service; [Atlanta: for loan by National Medical Audiovisual Center], 1965
- **Differential diagnosis of emphysema [videorecording]** Source: Washington Alaska Regional Medical Program; produced by Information & Education Resource Support Unit; Year: 1970; Format: Videorecording; [United States: s.n., 1970]
- **Emphysema [videorecording]** Source: Medfact; Year: 1976; Format: Videorecording; Massillon, Ohio: Medfact, [1976]
- **Emphysema [videorecording]** Source: [presented by] Medical Video Library; co-produced by IMS, Faculty of Medicine, University of Toronto and Medical Productions and Associates; Year: 1989; Format: Videorecording; [Toronto, Ont.]: Burn-Shield, [1989]
- **Living with emphysema [videorecording]: rehabilitation.** Year: 1989; Format: Videorecording; Boynton Beach, FL: Universal Health Communications, Inc., 1989
- **Living with emphysema. Part 3, Medical treatment [videorecording]** Source: [presented by] AIMS Media; a production of Health Communications Co; Year: 1989; Format: Videorecording; Boynton Beach, FL: Distributed by Universal Health Communications, c1989
- **Mrs. Fendi, a lady with emphysema [electronic resource]** Source: by Sharon Peirce Corbin; Year: 1992; Format: Electronic resource; Philadelphia, PA: J.B. Lippincott, c1992
- **Office management of chronic emphysema [videorecording]** Source: Washington Alaska Regional Medical Program; produced by Information & Education Resource Support Unit; Year: 1970; Format: Videorecording; [Seattle]: The Program, [1970]
- **Physiologic manifestations of emphysema [motion picture]** Source: [Rehabilitation Services Administration; produced by the U. S. Public Health Service]; Year: 1965; Format: Motion picture; [Washington: The Administration; Atlanta: for loan by National Medical Audiovisual Center], 1965
- **Reduction pneumonoplasty for emphysema [videorecording]: the VATS approach** Source: from the Film Library and the Clinical Congress of ACS; Year: 1996; Format: Videorecording; Woodbury, CT: Ciné-Med, [1996]
- **The Pathophysiology of emphysema [filmstrip]** Source: Trainex Corporation; Year: 1971; Format: Filmstrip; Garden Grove, Calif.: Trainex, c1971

CHAPTER 9. PERIODICALS AND NEWS ON EMPHYSEMA

Overview

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

News Services and Press Releases

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

- **Breathing-muscle training helps emphysema patients**
  Source: Reuters Health eLine
  Date: August 27, 2003
- **Medicare to pay for costly emphysema surgery**
  Source: Reuters Medical News
  Date: August 21, 2003

- **Surgery may help some emphysema patients: study**
  Source: Reuters Health eLine
  Date: May 20, 2003
- **Emphysema surgery may improve survival in some patients**
  Source: Reuters Medical News
  Date: May 20, 2003
- **Benefit of lung volume reduction surgery in severe emphysema persists long-term**
  Source: Reuters Medical News
  Date: April 18, 2003
- **Genetic risks of emphysema pinpointed in mice**
  Source: Reuters Health eLine
  Date: March 12, 2003
- **Aberrant TGF-beta signaling implicated in pathogenesis of emphysema**
  Source: Reuters Medical News
  Date: March 12, 2003
- **Bronchoscopic lung reduction successful in animal model of emphysema**
  Source: Reuters Medical News
  Date: March 10, 2003
- **Alpha, Baxter report FDA nod for hereditary emphysema therapy**
  Source: Reuters Industry Breifing
  Date: January 09, 2003
- **Aventis Behring seeks US approval for hereditary emphysema treatment**
  Source: Reuters Industry Breifing
  Date: January 06, 2003
- **Baxter to buy Alpha's hereditary emphysema drug, plasma-collection operations**
  Source: Reuters Industry Breifing
  Date: December 20, 2002
- **Body mass index is associated with asthma, emphysema, chronic bronchitis**
  Source: Reuters Medical News
  Date: November 20, 2002
- **Some asthmatic children may show emphysema-like lung changes**
  Source: Reuters Medical News
  Date: August 06, 2002
- **Surgical selection criteria for lung cancer patients with emphysema may need revision**
  Source: Reuters Medical News
  Date: November 13, 2001
- **Lung surgery for emphysema questioned**
  Source: Reuters Health eLine
  Date: August 15, 2001
- **Aventis Behring's emphysema product given orphan drug status in Europe**
  Source: Reuters Industry Breifing
  Date: July 26, 2001
- **Long-term function improved after lung volume reduction surgery for emphysema**
  Source: Reuters Medical News
  Date: July 17, 2001

- **EMEA recommends orphan drug status for Bayer/PPL emphysema candidate**
  Source: Reuters Industry Breifing
  Date: May 29, 2001
- **Lung reduction surgery helps emphysema patients**
  Source: Reuters Health eLine
  Date: May 17, 2001
- **Lung volume reduction surgery benefits emphysema patients**
  Source: Reuters Medical News
  Date: May 14, 2001
- **PPL says sales of lead emphysema product could be worth $900 million**
  Source: Reuters Industry Breifing
  Date: March 16, 2001
- **Lung volume reduction provides good 5-year outcome for severe emphysema**
  Source: Reuters Medical News
  Date: October 26, 2000
- **Lung volume reduction improves pulmonary function in severe emphysema**
  Source: Reuters Medical News
  Date: October 25, 2000
- **Lung-volume-reduction surgery benefits some patients with severe emphysema**
  Source: Reuters Industry Breifing
  Date: July 27, 2000
- **Lung volume reduction surgery helps emphysema patients**
  Source: Reuters Health eLine
  Date: July 26, 2000
- **Bilateral lung reduction appears superior to unilateral operation for emphysema**
  Source: Reuters Medical News
  Date: July 12, 2000

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

Academic Periodicals covering Emphysema

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

Alpha 1 -Proteinase Inhibitor, Human

- **Systemic - U.S. Brands:** Prolastin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202022.html

Benzonatate

- **Systemic - U.S. Brands:** Tessalon
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202085.html

Bronchodilators, Adrenergic

- **Inhalation - U.S. Brands:** Adrenalin Chloride; Airet; Alupent; Arm-a-Med Isoetharine; Arm-a-Med Metaproterenol; Asthmahaler Mist; AsthmaNefrin; Beta-2; Brethaire; Bronkaid Mist; Bronkaid Suspension Mist; Bronkometer; Bronkosol; Dey-Lute Isoetharine; Dey-Lute Metaproterenol
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202095.html
- **Oral/Injection - U.S.** Brands: Adrenalin; Alupent; Ana-Guard; Brethine; Bricanyl; EpiPen Auto-Injector; EpiPen Jr. Auto-Injector; Isuprel; Proventil; Proventil Repetabs; Ventolin; Volmax
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202096.html

Bronchodilators, Theophylline

- **Systemic - U.S. Brands:** Aerolate Sr; Asmalix; Choledyl; Choledyl SA; Elixophyllin; Lanophyllin; Phyllocontin; Quibron-T Dividose; Quibron-T/SR Dividose; Respbid; Slo-Bid Gyrocaps; Slo-Phyllin; Theo-24; Theobid Duracaps; Theochron; Theo-Dur; Theolair; Theolair-SR; Theo-Time
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/201945.html

Corticosteroids

- **Dental - U.S. Brands:** Kenalog in Orabase; Orabase-HCA; Oracort; Oralone
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202010.html
- **Inhalation - U.S. Brands:** AeroBid; AeroBid-M; Azmacort; Beclovent; Decadron Respihaler; Pulmicort Respules; Pulmicort Turbuhaler; Vanceril; Vanceril 84 mcg Double Strength
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202011.html
- **Nasal - U.S. Brands:** Beconase; Beconase AQ; Dexacort Turbinaire; Flonase; Nasacort; Nasacort AQ; Nasalide; Nasarel; Nasonex; Rhinocort; Vancenase; Vancenase AQ 84 mcg; Vancenase pockethaler
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202012.html
- **Ophthalmic - U.S. Brands:** AK-Dex; AK-Pred; AK-Tate; Baldex; Decadron; Dexair; Dexotic; Econopred; Econopred Plus; Eflone; Flarex; Fluor-Op; FML Forte; FML Liquifilm; FML S.O.P.; HMS Liquifilm; Inflamase Forte; Inflamase Mild; I-Pred; Lite Pred; Maxidex; Ocu-Dex; Ocu-Pred
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202013.html
- **Otic - U.S. Brands:** Decadron
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202014.html

- **Rectal - U.S. Brands:** Anucort-HC; Anu-Med HC; Anuprep HC; Anusol-HC; Anutone-HC; Anuzone-HC; Cort-Dome; Cortenema; Cortifoam; Hemorrhoidal HC; Hemril-HC Uniserts; Proctocort; Proctosol-HC; Rectosol-HC
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203366.html

Dextromethorphan

- **Systemic - U.S. Brands:** Cough-X; Creo-Terpin; Trocal
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202187.html

Dyphylline

- **Systemic - U.S. Brands:** Dilor; Dilor-400; Lufyllin; Lufyllin-400
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202752.html

Ipratropium

- **Inhalation - U.S. Brands:** Atrovent
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202304.html

Ipratropium and Albuterol

- **Inhalation-Local - U.S.** Brands: Combivent; DuoNeb
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203487.html

Oxtriphylline and Guaifenesin

- **Systemic - U.S. Brands:** Brondelate
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202430.html

Theophylline and Guaifenesin

- **Systemic - U.S. Brands:** Bronchial; Elixophyllin-GG; Glyceryl-T; Quibron; Quibron-300; Theocon; Theolate
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202557.html

Theophylline, Ephedrine, and Hydroxyzine

- **Systemic - U.S. Brands:** Marax; Marax-DF
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202555.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 emphysema 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 "emphysema" (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 emphysema:

- **recombinant human alpha-1 antitrypsin (rAAT) (trade name: NONE Assigned)**
  http://www.rarediseases.org/nord/search/nodd_full?code=1197
- **Alpha1-proteinase inhibitor (human)**
  http://www.rarediseases.org/nord/search/nodd_full?code=1003
- **hyaluronic acid (trade name: NONE Assigned)**
  http://www.rarediseases.org/nord/search/nodd_full?code=1244
- **hyaluronic acid**
  http://www.rarediseases.org/nord/search/nodd_full?code=1272

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**

---

[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 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 "emphysema" (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	19745
Books / Periodicals / Audio Visual	307
Consumer Health	715
Meeting Abstracts	19
Other Collections	2
Total	20788

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 "emphysema" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

---

[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).

[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.

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 general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

The Genome Project and Emphysema

In the following section, we will discuss databases and references which relate to the Genome Project and emphysema.

Online Mendelian Inheritance in Man (OMIM)

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).[23] The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

---

[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.

[23] Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

To search the database, go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html**. Type "emphysema" (or synonyms) into the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. In particular, the option "Database Links" will search across technical databases that offer an abundance of information. The following is an example of the results you can obtain from the OMIM for emphysema:

- **Berry Aneurysm, Cirrhosis, Pulmonary Emphysema, and Cerebral Calcification**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?210050
- **Emphysema, Congenital Lobar**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?130710
- **Emphysema, Congenital, with Deafness, Penoscrotal Web, and Mental Retardation**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?602564
- **Emphysema, Hereditary Pulmonary**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?130700
- **Hemolytic Anemia, Congenital, with Emphysema and Cutis Laxa**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?235360

Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web site categorizes each disorder by system of the body. Go to **http://www.ncbi.nlm.nih.gov/disease/**, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to revisit it from time to time. The following systems and associated disorders are addressed:

- **Cancer:** Uncontrolled cell division.
  Examples: Breast and ovarian cancer, Burkitt lymphoma, chronic myeloid leukemia, colon cancer, lung cancer, malignant melanoma, multiple endocrine neoplasia, neurofibromatosis, p53 tumor suppressor, pancreatic cancer, prostate cancer, Ras oncogene, RB: retinoblastoma, von Hippel-Lindau syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Cancer.html**
- **Immune System:** Fights invaders.
  Examples: Asthma, autoimmune polyglandular syndrome, Crohn's disease, DiGeorge syndrome, familial Mediterranean fever, immunodeficiency with Hyper-IgM, severe combined immunodeficiency.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Immune.html**
- **Metabolism:** Food and energy.
  Examples: Adreno-leukodystrophy, atherosclerosis, Best disease, Gaucher disease, glucose galactose malabsorption, gyrate atrophy, juvenile-onset diabetes, obesity, paroxysmal nocturnal hemoglobinuria, phenylketonuria, Refsum disease, Tangier disease, Tay-Sachs disease.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Metabolism.html**
- **Muscle and Bone:** Movement and growth.
  Examples: Duchenne muscular dystrophy, Ellis-van Creveld syndrome, Marfan

syndrome, myotonic dystrophy, spinal muscular atrophy.
Web site: **http://www.ncbi.nlm.nih.gov/disease/Muscle.html**

- **Nervous System:** Mind and body.
  Examples: Alzheimer disease, amyotrophic lateral sclerosis, Angelman syndrome, Charcot-Marie-Tooth disease, epilepsy, essential tremor, fragile X syndrome, Friedreich's ataxia, Huntington disease, Niemann-Pick disease, Parkinson disease, Prader-Willi syndrome, Rett syndrome, spinocerebellar atrophy, Williams syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Brain.html**
- **Signals:** Cellular messages.
  Examples: Ataxia telangiectasia, Cockayne syndrome, glaucoma, male-patterned baldness, SRY: sex determination, tuberous sclerosis, Waardenburg syndrome, Werner syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Signals.html**
- **Transporters:** Pumps and channels.
  Examples: Cystic fibrosis, deafness, diastrophic dysplasia, Hemophilia A, long-QT syndrome, Menkes syndrome, Pendred syndrome, polycystic kidney disease, sickle cell anemia, Wilson's disease, Zellweger syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Transporters.html**

Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **3D Domains:** Domains from Entrez Structure,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Books:** Online books,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books**
- **Genome:** Complete genome assemblies,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome**
- **NCBI's Protein Sequence Information Survey Results:**
  Web site: **http://www.ncbi.nlm.nih.gov/About/proteinsurvey/**
- **Nucleotide Sequence Database (Genbank):**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide**
- **OMIM:** Online Mendelian Inheritance in Man,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**
- **PopSet:** Population study data sets,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset**
- **ProbeSet:** Gene Expression Omnibus (GEO),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Protein Sequence Database:**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein**

- **PubMed:** Biomedical literature (PubMed),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed**
- **Structure:** Three-dimensional macromolecular structures,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure**
- **Taxonomy:** Organisms in GenBank,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy**

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=genome**, and then select the database that you would like to search. The databases available are listed in the drop box next to "Search." Enter "emphysema" (or synonyms) into the search box and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[24]

This online resource has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually limited or completely omitted in existing reference sources due to space limitations of the printed form.

At **http://www.nlm.nih.gov/mesh/jablonski/syndrome_toc/toc_a.html**, you can search across syndromes using an alphabetical index**.** Search by keywords at **http://www.nlm.nih.gov/mesh/jablonski/syndrome_db.html**.

The Genome Database[25]

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

---

[24] Adapted from the National Library of Medicine:
http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html.

[25] Adapted from the Genome Database: **http://gdbwww.gdb.org/gdb/aboutGDB.html - mission**.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type "emphysema" (or synonyms) into the search box, and review the results. If more than one word is used in the search box, then separate each one with the word "and" or "or" (using "or" might be useful when using synonyms).

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 emphysema 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 emphysema. 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 emphysema. 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 "emphysema":

- Guides on emphysema

  Emphysema
  http://www.nlm.nih.gov/medlineplus/emphysema.html

- Other guides

  Alpha-1 Antitrypsin Deficiency
  http://www.nlm.nih.gov/medlineplus/alpha1antitrypsindeficiency.html

  Bronchitis
  http://www.nlm.nih.gov/medlineplus/bronchitis.html

  Chronic Obstructive Pulmonary Disease
  http://www.nlm.nih.gov/medlineplus/tutorials/copdloader.html

  COPD
  http://www.nlm.nih.gov/medlineplus/copdchronicobstructivepulmonarydisease.html

  Respiratory Diseases
  http://www.nlm.nih.gov/medlineplus/respiratorydiseases.html

Within the health topic page dedicated to emphysema, the following was listed:

- Diagnosis/Symptoms

  Lung - Diagnosis of COPD and Asthma
  Source: National Lung Health Education Program
  http://www.nlhep.org/lung_diagnosis.html

  Spirometry
  Source: National Lung Health Education Program
  http://www.nlhep.org/spirom1.html

- Treatment

  Lung - Treatment of COPD and Asthma
  Source: National Lung Health Education Program
  http://www.nlhep.org/lung_trtmnt.html

- Specific Conditions/Aspects

  Alpha-1 Related Emphysema
  Source: American Lung Association
  http://www.lungusa.org/diseases/luna1ad.html

  Emphysema: Does It Increase the Risk of Lung Cancer?
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=HQ00617

- Organization

  American Lung Association
  http://www.lungusa.org/

National Emphysema Foundation
http://emphysemafoundation.org/

National Heart, Lung, and Blood Institute
http://www.nhlbi.nih.gov/

National Lung Health Education Program
http://www.nlhep.org/

- Research

  Landmark Cooperative Federal Study Defines the Role of Lung Surgery in the Treatment of Severe Emphysema
  Source: National Heart, Lung, and Blood Institute
  http://www.nih.gov/news/pr/may2003/nhlbi-20.htm

  NHLBI-Funded Emphysema Study Finds Certain Patients at High Risk for Death Following Lung Surgery
  Source: National Heart, Lung, and Blood Institute
  http://www.nih.gov/news/pr/aug2001/nhlbi-14.htm

- Statistics

  FASTATS: Emphysema
  Source: Centers for Disease Control and Prevention
  http://www.cdc.gov/nchs/fastats/emphsema.htm

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 emphysema. 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:

- **Cigars: More Dangerous Than You Think**

  Source: South Deerfield, MA: Channing L. Bete Co., Inc. 1999. 15 p.

  Contact: Available from Channing L. Bete Co., Inc. 200 State Road, South Deerfield, MA 01373. (800) 628-7733. Fax (800) 499-6464. E-mail: custsvcs@channing-bete.com. Website: www.channing-bete.com. PRICE: $1.05 for 1-99 copies; bulk copies available. Item number 73958B-01-99.

Summary: This booklet describes the health hazards associated with smoking cigars. Contrary to a popular myth that cigar smoking is a harmless habit, the booklet explains that cigars can be addictive because of their nicotine content. The booklet explores why people start smoking cigars; the publicity and imaging that surrounds cigars and cigar users; how smoking causes cancer of the mouth, larynx, esophagus, and lungs; other risks associated with smoking cigars, including **emphysema** and chronic bronchitis, heart disease, and nicotine addiction; the problem of secondhand cigar smoke; and the impact of cigar smoking on one's breath, teeth, hair, clothes, and home. The booklet includes a section of ideas on how to handle a variety of situations where smoking may be encountered; and another section on tips for quitting cigar smoking. One sidebar lists the telephone numbers for some organizations through which readers can get more information. The brochure is illustrated with line drawings of a variety of people, depicted in everyday settings.

- **Tobacco-Free For Life!**

  Source: Kansas City, MO: School of Dentistry, University of Missouri-Kansas City. May 1995. [19 p.].

  Contact: Available from University of Missouri-Kansas City. School of Dentistry, 650 East 25th Street, Kansas City, MO 64108-2784. (816) 235-2160. PRICE: Single copy free.

  Summary: This booklet focuses on tobacco addiction and on how to quit using tobacco products. It explains why people use tobacco and why it is difficult for people to quit. It lists reasons why tobacco users should quit. By quitting, tobacco users can have better health, including cleaner teeth, fresher breath, healthier gums, fewer colds, better taste and smell, easier breathing, and can also lower the risk for serious health problems such as cancer, **emphysema,** heart disease, and stroke. After explaining the problems smoking causes, the booklet offers suggestions on how to quit using tobacco. It describes withdrawal symptoms that may be expected and offers suggestions on how to relieve these symptoms. The booklet also covers spit tobacco. It warns that spit tobacco is not a safe alternative to cigarettes and can cause bad breath, stained teeth, loss of teeth from gum disease, and cancer. A pinch of spit tobacco has the same amount of nicotine as 2.5 cigarettes and can be more addicting than cigarettes. The booklet is filled with colorful, cartoon-like line drawings.

- **Basics of Alpha 1-Antitrypsin Deficiency**

  Source: Minneapolis, MN: Alpha 1 Association. 1999. [4 p.].

  Contact: Available from Alpha 1 Association. 8120 Penn Avenue, South, Suite 549, Minneapolis, MN 55431-1326. (800) 521-3025 or (612) 703-9979. Fax (612) 703-9977. E-mail: A1NA@alpha1.org. Website: www.alpha1.org. PRICE: $0.25 plus shipping and handling; bulk copies available.

  Summary: This brochure describes Alpha 1 antitrypsin deficiency (A1AD or Alpha 1), a genetic disorder that affects infants, children, and adults. It is the most common metabolic disorder that causes liver disease in infants and children; the disorder also causes cirrhosis and cancer of the liver in adults. The brochure reviews the functions of the liver, the causes of the deficiency, modes of inheritance, screening for A1AD, and symptoms in children and adults (including lung and liver disease and a skin disease called panniculitis). Alpha 1 antitrypsin (AAT) is a protein primarily manufactured in the liver and then released into the blood. The normal function of AAT is to protect body tissues from being damaged by neutrophil elastase, a protein found in white blood cells. The backup of abnormal AAT in the liver can cause liver damage. Screening for

A1AD is done through a simple blood test. Lung disease is the most common manifestation of A1AD, with **emphysema** the most prevalent of the lung diseases. Liver disease is the second most common manifestation of AAT deficiency; it may cause chronic hepatitis or cirrhosis. No specific therapy for A1AD liver disease is available but rather involves supportive management for liver dysfunction and prevention of complications. Liver transplantation may be recommended for severe liver disease. The brochure concludes with contact information for the Alpha 1 Association and a form readers can request more information. 1 figure. 4 references.

- **Clinic: Specialized Care for Respiratory Disease in an Outpatient Setting**

  Source: Denver, CO: National Jewish Center for Immunology and Respiratory Medicine. 1992. 8 p.

  Contact: Available from National Jewish Center for Immunology and Respiratory Medicine. Department of Medicine, 1400 Jackson Street, Denver, CO 80206. (800) 222-5864 or (303) 398-1571. PRICE: Single copy free.

  Summary: This brochure describes the Cohen Clinic of the National Jewish Center for Immunology and Respiratory Medicine, a non-sectarian medical center dedicated entirely to the treatment and research of chronic respiratory, allergic, and immunologic disease in adults and children; the Cohen Clinic provides medical care in an outpatient setting. The brochure describes patient care, the COPE Program, pediatric care, the **emphysema** program, and the pulmonary rehabilitation program of the Clinic. Communication-related disorders that are included in the Clinic's care include vocal cord dysfunction and chronic sinus disease. The brochure concludes with a list of specialties of the physicians staffing the clinic, and with information about insurance, and making appointments.

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:

- **A1AD Related Emphysema**

  Summary: This online consumer health information fact sheet provides basic information about this respiratory disorder which is caused by an inherited lack of a protective protein called alpha1-antitrypsin

  Source: American Lung Association

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=2470

- **Emphysema**

  Summary: Online consumer health information about this respiratory disorder -- includes a description of the disease, causes and symptoms, treatment options and information on current research.

  Source: American Lung Association

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=2473

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 emphysema. 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 emphysema. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with emphysema.

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 emphysema. 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 "emphysema" (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 "emphysema". 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 "emphysema" (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 "emphysema" (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.[26]

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

[26] 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)[27]:

- **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/**

[27] 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 emphysema:

- **Basic Guidelines for Emphysema**

  Emphysema
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000136.htm

- **Signs & Symptoms for Emphysema**

  Ankle, feet, and leg swelling
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003104.htm

  Anxiety, stress, and tension
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003211.htm

  Bluish coloration of the skin
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003215.htm

  Breath sounds
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003323.htm

Breathing difficulty
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003075.htm

Breathing difficulty, lying down
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003076.htm

Clubbing of the fingers or toes
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003282.htm

Cough
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003072.htm

Difficulty falling asleep
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003210.htm

Dizziness
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003093.htm

Excessive daytime sleepiness
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003208.htm

Eyes, bulging
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003033.htm

Fatigue
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003088.htm

Headache
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003024.htm

Impotence
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003164.htm

Insomnia
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003210.htm

Leg swelling
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003104.htm

Lung disease
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000066.htm

Memory loss
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003257.htm

Nasal flaring
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003055.htm

Rales
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003323.htm

Shortness of breath
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003075.htm

Stress
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003211.htm

Swelling
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003103.htm

Tension
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003211.htm

Vision abnormalities
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003029.htm

Weight loss
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003107.htm

Wheezing
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003070.htm

- **Diagnostics and Tests for Emphysema**

ALP
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003470.htm

Alpha-1 antitrypsin
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003715.htm

ALT
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003473.htm

Arterial blood gases
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003855.htm

Blood gases
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003855.htm

CEA
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003574.htm

Chest MRI
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003794.htm

Chest X-ray
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003804.htm

MRI
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003335.htm

Pulmonary function tests
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003853.htm

Pulmonary ventilation/perfusion scan
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003828.htm

Serum alpha-1 antitrypsin level
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003715.htm

Urine pH
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003583.htm

X-ray
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003337.htm

- **Background Topics for Emphysema**

Chronic
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002312.htm

Cigarette smoking
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002032.htm

Incidence
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002387.htm

Physical examination
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002274.htm

Respiratory
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002290.htm

Smoking
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002032.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**

EMPHYSEMA 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]

Abducens: A striated, extrinsic muscle of the eyeball that originates from the annulus of Zinn. [NIH]

Abducens Nerve: The 6th cranial nerve. The abducens nerve originates in the abducens nucleus of the pons and sends motor fibers to the lateral rectus muscles of the eye. Damage to the nerve or its nucleus disrupts horizontal eye movement control. [NIH]

Abducens Nerve Diseases: Diseases of the sixth cranial (abducens) nerve or its nucleus in the pons. The nerve may be injured along its course in the pons, intracranially as it travels along the base of the brain, in the cavernous sinus, or at the level of superior orbital fissure or orbit. Dysfunction of the nerve causes lateral rectus muscle weakness, resulting in horizontal diplopia that is maximal when the affected eye is abducted and esotropia. Common conditions associated with nerve injury include intracranial hypertension; craniocerebral trauma; ischemia; and infratentorial neoplasms. [NIH]

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

Abrasion: 1. The wearing away of a substance or structure (such as the skin or the teeth) through some unusual or abnormal mechanical process. 2. An area of body surface denuded of skin or mucous membrane by some unusual or abnormal mechanical process. [EU]

Abscess: Accumulation of purulent material in tissues, organs, or circumscribed spaces, usually associated with signs of infection. [NIH]

Acceptor: A substance which, while normally not oxidized by oxygen or reduced by hydrogen, can be oxidized or reduced in presence of a substance which is itself undergoing oxidation or reduction. [NIH]

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]

Activities of Daily Living: The performance of the basic activities of self care, such as dressing, ambulation, eating, etc., in rehabilitation. [NIH]

Acylation: The addition of an organic acid radical into a molecule. [NIH]

Adaptability: Ability to develop some form of tolerance to conditions extremely different

from those under which a living organism evolved. [NIH]

Adaptation: 1. The adjustment of an organism to its environment, or the process by which it enhances such fitness. 2. The normal ability of the eye to adjust itself to variations in the intensity of light; the adjustment to such variations. 3. The decline in the frequency of firing of a neuron, particularly of a receptor, under conditions of constant stimulation. 4. In dentistry, (a) the proper fitting of a denture, (b) the degree of proximity and interlocking of restorative material to a tooth preparation, (c) the exact adjustment of bands to teeth. 5. In microbiology, the adjustment of bacterial physiology to a new environment. [EU]

Adenine: A purine base and a fundamental unit of adenine nucleotides. [NIH]

Adenocarcinoma: A malignant epithelial tumor with a glandular organization. [NIH]

Adenosine: A nucleoside that is composed of adenine and d-ribose. Adenosine or adenosine derivatives play many important biological roles in addition to being components of DNA and RNA. Adenosine itself is a neurotransmitter. [NIH]

Adhesions: Pathological processes consisting of the union of the opposing surfaces of a wound. [NIH]

Adipose Tissue: Connective tissue composed of fat cells lodged in the meshes of areolar tissue. [NIH]

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

Adjuvant: A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

Adjuvant Therapy: Treatment given after the primary treatment to increase the chances of a cure. Adjuvant therapy may include chemotherapy, radiation therapy, or hormone therapy. [NIH]

Adsorption: The condensation of gases, liquids, or dissolved substances on the surfaces of solids. It includes adsorptive phenomena of bacteria and viruses as well as of tissues treated with exogenous drugs and chemicals. [NIH]

Adsorptive: It captures volatile compounds by binding them to agents such as activated carbon or adsorptive resins. [NIH]

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

Aerobic: In biochemistry, reactions that need oxygen to happen or happen when oxygen is present. [NIH]

Aerosol: A solution of a drug which can be atomized into a fine mist for inhalation therapy. [EU]

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]

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]

Air Sacs: Thin-walled sacs or spaces which function as a part of the respiratory system in birds, fishes, insects, and mammals. [NIH]

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

Airway Obstruction: Any hindrance to the passage of air into and out of the lungs. [NIH]

Albumin: 1. Any protein that is soluble in water and moderately concentrated salt solutions and is coagulable by heat. 2. Serum albumin; the major plasma protein (approximately 60 per cent of the total), which is responsible for much of the plasma colloidal osmotic pressure and serves as a transport protein carrying large organic anions, such as fatty acids, bilirubin, and many drugs, and also carrying certain hormones, such as cortisol and thyroxine, when their specific binding globulins are saturated. Albumin is synthesized in the liver. Low serum levels occur in protein malnutrition, active inflammation and serious hepatic and renal disease. [EU]

Aldehydes: Organic compounds containing a carbonyl group in the form -CHO. [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]

Alkaloid: A member of a large group of chemicals that are made by plants and have nitrogen in them. Some alkaloids have been shown to work against cancer. [NIH]

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

Allergen: An antigenic substance capable of producing immediate-type hypersensitivity (allergy). [EU]

Allergic Rhinitis: Inflammation of the nasal mucous membrane associated with hay fever; fits may be provoked by substances in the working environment. [NIH]

Alpha 1-Antichymotrypsin: Glycoprotein found in alpha(1)-globulin region in human serum. It inhibits chymotrypsin-like proteinases in vivo and has cytotoxic killer-cell activity in vitro. The protein also has a role as an acute-phase protein and is active in the control of immunologic and inflammatory processes, and as a tumor marker. It is a member of the serpin superfamily. [NIH]

Alpha 1-Antitrypsin: Plasma glycoprotein member of the serpin superfamily which inhibits trypsin, neutrophil elastase, and other proteolytic enzymes. Commonly referred to as alpha 1-proteinase inhibitor (A1PI), it exists in over 30 different biochemical variant forms known collectively as the PI (protease inhibitor) system. Hereditary A1PI deficiency is associated with pulmonary emphysema. [NIH]

Alpha 1-Antitrypsin Deficiency: A disease caused by single gene defects. [NIH]

Alpha Particles: Positively charged particles composed of two protons and two neutrons, i.e., helium nuclei, emitted during disintegration of very heavy isotopes; a beam of alpha particles or an alpha ray has very strong ionizing power, but weak penetrability. [NIH]

Alpha-1: A protein with the property of inactivating proteolytic enzymes such as leucocyte collagenase and elastase. [NIH]

Alternative medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used instead of standard treatments.

Alternative medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Alveolar Process: The thickest and spongiest part of the maxilla and mandible hollowed out into deep cavities for the teeth. [NIH]

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

Alveolitis: Inflammation of an alveolus. Called also odontobothritis. [EU]

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

Amenorrhea: Absence of menstruation. [NIH]

Amino Acid Sequence: The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

Amino Acid Substitution: The naturally occurring or experimentally induced replacement of one or more amino acids in a protein with another. If a functionally equivalent amino acid is substituted, the protein may retain wild-type activity. Substitution may also diminish or eliminate protein function. Experimentally induced substitution is often used to study enzyme activities and binding site properties. [NIH]

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

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

Amiodarone: An antianginal and antiarrhythmic drug. It increases the duration of ventricular and atrial muscle action by inhibiting Na,K-activated myocardial adenosine triphosphatase. There is a resulting decrease in heart rate and in vascular resistance. [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]

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

Amplification: The production of additional copies of a chromosomal DNA sequence, found as either intrachromosomal or extrachromosomal DNA. [NIH]

Ampulla: A sac-like enlargement of a canal or duct. [NIH]

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]

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]

Aneurysm: A sac formed by the dilatation of the wall of an artery, a vein, or the heart. [NIH]

Angina: Chest pain that originates in the heart. [NIH]

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]

Angioplasty: Endovascular reconstruction of an artery, which may include the removal of atheromatous plaque and/or the endothelial lining as well as simple dilatation. These are procedures performed by catheterization. When reconstruction of an artery is performed surgically, it is called endarterectomy. [NIH]

Angiotensinogen: An alpha-globulin of which a fragment of 14 amino acids is converted by renin to angiotensin I, the inactive precursor of angiotensin II. It is a member of the serpin superfamily. [NIH]

Animal model: An animal with a disease either the same as or like a disease in humans. Animal models are used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models. [NIH]

Anions: Negatively charged atoms, radicals or groups of atoms which travel to the anode or positive pole during electrolysis. [NIH]

Anisotropy: A physical property showing different values in relation to the direction in or along which the measurement is made. The physical property may be with regard to thermal or electric conductivity or light refraction. In crystallography, it describes crystals whose index of refraction varies with the direction of the incident light. It is also called acolotropy and colotropy. The opposite of anisotropy is isotropy wherein the same values characterize the object when measured along axes in all directions. [NIH]

Annealing: The spontaneous alignment of two single DNA strands to form a double helix. [NIH]

Anorexia: Lack or loss of appetite for food. Appetite is psychologic, dependent on memory and associations. Anorexia can be brought about by unattractive food, surroundings, or company. [NIH]

Anorexia Nervosa: The chief symptoms are inability to eat, weight loss, and amenorrhea. [NIH]

Antianginal: Counteracting angina or anginal conditions. [EU]

Antiarrhythmic: An agent that prevents or alleviates cardiac arrhythmia. [EU]

Antibacterial: A substance that destroys bacteria or suppresses their growth or reproduction. [EU]

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

Antibodies: Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the antigen that induced their synthesis in cells of the lymphoid series (especially plasma cells), or with an antigen closely related to it. [NIH]

Antibody: A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. [NIH]

Antibody therapy: Treatment with an antibody, a substance that can directly kill specific tumor cells or stimulate the immune system to kill tumor cells. [NIH]

Anticoagulant: A drug that helps prevent blood clots from forming. Also called a blood thinner. [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]

Anti-infective: An agent that so acts. [EU]

Anti-inflammatory: Having to do with reducing inflammation. [NIH]

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

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]

Antiplasmin: A member of the serpin superfamily found in human plasma that inhibits the lysis of fibrin clots which are induced by plasminogen activator. It is a glycoprotein, molecular weight approximately 70,000 that migrates in the alpha 2 region in immunoelectrophoresis. It is the principal plasmin inactivator in blood, rapidly forming a very stable complex with plasmin. [NIH]

Antiseptic: A substance that inhibits the growth and development of microorganisms without necessarily killing them. [EU]

Antiserum: The blood serum obtained from an animal after it has been immunized with a particular antigen. It will contain antibodies which are specific for that antigen as well as antibodies specific for any other antigen with which the animal has previously been immunized. [NIH]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Anuria: Inability to form or excrete urine. [NIH]

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

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

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

Aortic Aneurysm: Aneurysm of the aorta. [NIH]

Aplastic anemia: A condition in which the bone marrow is unable to produce blood cells. [NIH]

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

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

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

Aqueous: Having to do with water. [NIH]

Aqueous humor: Clear, watery fluid that flows between and nourishes the lens and the cornea; secreted by the ciliary processes. [NIH]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Argon: A noble gas with the atomic symbol Ar, atomic number 18, and atomic weight 39.948. It is used in fluorescent tubes and wherever an inert atmosphere is desired and nitrogen cannot be used. [NIH]

Aromatic: Having a spicy odour. [EU]

Arrestin: A 48-Kd protein of the outer segment of the retinal rods and a component of the phototransduction cascade. Arrestin quenches G-protein activation by binding to phosphorylated photolyzed rhodopsin. Arrestin causes experimental autoimmune uveitis when injected into laboratory animals. [NIH]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arteriolar: Pertaining to or resembling arterioles. [EU]

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Arteriolosclerosis: Sclerosis and thickening of the walls of the smaller arteries (arterioles). Hyaline arteriolosclerosis, in which there is homogeneous pink hyaline thickening of the arteriolar walls, is associated with benign nephrosclerosis. Hyperplastic arteriolosclerosis, in which there is a concentric thickening with progressive narrowing of the lumina may be associated with malignant hypertension, nephrosclerosis, and scleroderma. [EU]

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

Arteriosus: Circle composed of anastomosing arteries derived from two long posterior ciliary and seven anterior ciliary arteries, located in the ciliary body about the root of the iris. [NIH]

Arthroscopy: Endoscopic examination, therapy and surgery of the joint. [NIH]

Ascites: Accumulation or retention of free fluid within the peritoneal cavity. [NIH]

Ascorbic Acid: A six carbon compound related to glucose. It is found naturally in citrus fruits and many vegetables. Ascorbic acid is an essential nutrient in human diets, and necessary to maintain connective tissue and bone. Its biologically active form, vitamin C, functions as a reducing agent and coenzyme in several metabolic pathways. Vitamin C is considered an antioxidant. [NIH]

Aspiration: The act of inhaling. [NIH]

Aspirin: A drug that reduces pain, fever, inflammation, and blood clotting. Aspirin belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is also being studied in cancer prevention. [NIH]

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

Astringent: Causing contraction, usually locally after topical application. [EU]

Astrocytes: The largest and most numerous neuroglial cells in the brain and spinal cord. Astrocytes (from "star" cells) are irregularly shaped with many long processes, including those with "end feet" which form the glial (limiting) membrane and directly and indirectly contribute to the blood brain barrier. They regulate the extracellular ionic and chemical environment, and "reactive astrocytes" (along with microglia) respond to injury. Astrocytes have high- affinity transmitter uptake systems, voltage-dependent and transmitter-gated ion channels, and can release transmitter, but their role in signaling (as in many other functions) is not well understood. [NIH]

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Asynchronous: Pacing mode where only one timing interval exists, that between the stimuli. While the duration of this interval may be varied, it is not modified by any sensed event once set. As no sensing occurs, the upper and lower rate intervals are the same as the pacema. [NIH]

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

Atelectasis: Incomplete expansion of the lung. [NIH]

Atmospheric Pressure: The pressure at any point in an atmosphere due solely to the weight of the atmospheric gases above the point concerned. [NIH]

Atopic: Pertaining to an atopen or to atopy; allergic. [EU]

Atresia: Lack of a normal opening from the esophagus, intestines, or anus. [NIH]

Atrial: Pertaining to an atrium. [EU]

Atrophy: Decrease in the size of a cell, tissue, organ, or multiple organs, associated with a variety of pathological conditions such as abnormal cellular changes, ischemia, malnutrition, or hormonal changes. [NIH]

Attenuated: Strain with weakened or reduced virulence. [NIH]

Attenuation: Reduction of transmitted sound energy or its electrical equivalent. [NIH]

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

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]

Autologous: Taken from an individual's own tissues, cells, or DNA. [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]

Autopsy: Postmortem examination of the body. [NIH]

Autoradiography: A process in which radioactive material within an object produces an image when it is in close proximity to a radiation sensitive emulsion. [NIH]

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

Axons: Nerve fibers that are capable of rapidly conducting impulses away from the neuron cell body. [NIH]

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]

Bactericidal: Substance lethal to bacteria; substance capable of killing bacteria. [NIH]

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

Basal Ganglia: Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [NIH]

Basal Ganglia Diseases: Diseases of the basal ganglia including the putamen; globus pallidus; claustrum; amygdala; and caudate nucleus. Dyskinesias (most notably involuntary movements and alterations of the rate of movement) represent the primary clinical manifestations of these disorders. Common etiologies include cerebrovascular disease; neurodegenerative diseases; and craniocerebral trauma. [NIH]

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

Base Sequence: The sequence of purines and pyrimidines in nucleic acids and polynucleotides. It is also called nucleotide or nucleoside sequence. [NIH]

Basement Membrane: Ubiquitous supportive tissue adjacent to epithelium and around smooth and striated muscle cells. This tissue contains intrinsic macromolecular components such as collagen, laminin, and sulfated proteoglycans. As seen by light microscopy one of its subdivisions is the basal (basement) lamina. [NIH]

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]

Beta-Thromboglobulin: A platelet-specific protein which is released when platelets aggregate. Elevated plasma levels have been reported after deep venous thrombosis, pre-eclampsia, myocardial infarction with mural thrombosis, and myeloproliferative disorders. Measurement of beta-thromboglobulin in biological fluids by radioimmunoassay is used for the diagnosis and assessment of progress of thromboembolic disorders. [NIH]

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 Pigments: Pigments that give a characteristic color to bile including: bilirubin, biliverdine, and bilicyanin. [NIH]

Biliary: Having to do with the liver, bile ducts, and/or gallbladder. [NIH]

Biliary Tract: The gallbladder and its ducts. [NIH]

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

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

Biological response modifier: BRM. A substance that stimulates the body's response to infection and disease. [NIH]

Biological therapy: Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier (BRM) therapy. [NIH]

Biological Transport: The movement of materials (including biochemical substances and drugs) across cell membranes and epithelial layers, usually by passive diffusion. [NIH]

Biomarkers: Substances sometimes found in an increased amount in the blood, other body fluids, or tissues and that may suggest the presence of some types of cancer. Biomarkers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and GI tract cancers), and PSA (prostate cancer). Also called tumor markers. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

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]

Bivalent: Pertaining to a group of 2 homologous or partly homologous chromosomes during the zygotene stage of prophase to the first metaphase in meiosis. [NIH]

Bladder: The organ that stores urine. [NIH]

Blood Coagulation: The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [NIH]

Blood Coagulation Factors: Endogenous substances, usually proteins, that are involved in the blood coagulation process. [NIH]

Blood Glucose: Glucose in blood. [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 Viscosity: The internal resistance of the blood to shear forces. The in vitro measure of whole blood viscosity is of limited clinical utility because it bears little relationship to the actual viscosity within the circulation, but an increase in the viscosity of circulating blood can contribute to morbidity in patients suffering from disorders such as sickle cell anemia and polycythemia. [NIH]

Blood Volume: Volume of circulating blood. It is the sum of the plasma volume and erythrocyte volume. [NIH]

Blot: To transfer DNA, RNA, or proteins to an immobilizing matrix such as nitrocellulose. [NIH]

Blotting, Western: Identification of proteins or peptides that have been electrophoretically separated by blotting and transferred to strips of nitrocellulose paper. The blots are then detected by radiolabeled antibody probes. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Body Mass Index: One of the anthropometric measures of body mass; it has the highest correlation with skinfold thickness or body density. [NIH]

Bolus: A single dose of drug usually injected into a blood vessel over a short period of time. Also called bolus infusion. [NIH]

Bolus infusion: A single dose of drug usually injected into a blood vessel over a short period of time. Also called bolus. [NIH]

Bone Density: The amount of mineral per square centimeter of bone. This is the definition used in clinical practice. Actual bone density would be expressed in grams per milliliter. It is most frequently measured by photon absorptiometry or x-ray computed tomography. [NIH]

Bone Marrow: The soft tissue filling the cavities of bones. Bone marrow exists in two types, yellow and red. Yellow marrow is found in the large cavities of large bones and consists mostly of fat cells and a few primitive blood cells. Red marrow is a hematopoietic tissue and is the site of production of erythrocytes and granular leukocytes. Bone marrow is made up of a framework of connective tissue containing branching fibers with the frame being filled with marrow cells. [NIH]

Bone Resorption: Bone loss due to osteoclastic activity. [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]

Brachytherapy: A collective term for interstitial, intracavity, and surface radiotherapy. It uses small sealed or partly-sealed sources that may be placed on or near the body surface or within a natural body cavity or implanted directly into the tissues. [NIH]

Bradykinin: A nonapeptide messenger that is enzymatically produced from kallidin in the blood where it is a potent but short-lived agent of arteriolar dilation and increased capillary permeability. Bradykinin is also released from mast cells during asthma attacks, from gut walls as a gastrointestinal vasodilator, from damaged tissues as a pain signal, and may be a neurotransmitter. [NIH]

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]

Breathing Exercises: Therapeutic exercises aimed to deepen inspiration or expiration or even to alter the rate and rhythm of respiration. [NIH]

Bronchi: The larger air passages of the lungs arising from the terminal bifurcation of the trachea. [NIH]

Bronchial: Pertaining to one or more bronchi. [EU]

Bronchial Hyperreactivity: Tendency of the smooth muscle of the tracheobronchial tree to contract more intensely in response to a given stimulus than it does in the response seen in normal individuals. This condition is present in virtually all symptomatic patients with asthma. The most prominent manifestation of this smooth muscle contraction is a decrease in airway caliber that can be readily measured in the pulmonary function laboratory. [NIH]

Bronchiectasis: Persistent abnormal dilatation of the bronchi. [NIH]

Bronchiole: The smaller airways of the lungs. [NIH]

Bronchiolitis: Inflammation of the bronchioles. [NIH]

Bronchitis: Inflammation (swelling and reddening) of the bronchi. [NIH]

Bronchoalveolar Lavage: Washing out of the lungs with saline or mucolytic agents for diagnostic or therapeutic purposes. It is very useful in the diagnosis of diffuse pulmonary infiltrates in immunosuppressed patients. [NIH]

Bronchoalveolar Lavage Fluid: Fluid obtained by washout of the alveolar compartment of the lung. It is used to assess biochemical and inflammatory changes in and effects of therapy on the interstitial lung tissue. [NIH]

Bronchoconstriction: Diminution of the caliber of a bronchus physiologically or as a result of pharmacological intervention. [NIH]

Bronchodilator: A drug that relaxes the smooth muscles in the constricted airway. [NIH]

Bronchopulmonary: Pertaining to the lungs and their air passages; both bronchial and pulmonary. [EU]

Bronchopulmonary Dysplasia: A chronic lung disease appearing in certain newborn infants treated for respiratory distress syndrome with mechanical ventilation and elevated concentration of inspired oxygen. [NIH]

Bronchoscopy: Endoscopic examination, therapy or surgery of the bronchi. [NIH]

Bronchus: A large air passage that leads from the trachea (windpipe) to the lung. [NIH]

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

Bullous: Pertaining to or characterized by bullae. [EU]

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

Cachexia: General ill health, malnutrition, and weight loss, usually associated with chronic disease. [NIH]

Cadmium: An element with atomic symbol Cd, atomic number 48, and atomic weight 114. It is a metal and ingestion will lead to cadmium poisoning. [NIH]

Cadmium Poisoning: Poisoning occurring after exposure to cadmium compounds or fumes. It may cause gastrointestinal syndromes, anemia, or pneumonitis. [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]

Calculi: An abnormal concretion occurring mostly in the urinary and biliary tracts, usually composed of mineral salts. Also called stones. [NIH]

Capillary: Any one of the minute vessels that connect the arterioles and venules, forming a network in nearly all parts of the body. Their walls act as semipermeable membranes for the interchange of various substances, including fluids, between the blood and tissue fluid; called also vas capillare. [EU]

Capillary Permeability: Property of blood capillary walls that allows for the selective exchange of substances. Small lipid-soluble molecules such as carbon dioxide and oxygen move freely by diffusion. Water and water-soluble molecules cannot pass through the endothelial walls and are dependent on microscopic pores. These pores show narrow areas (tight junctions) which may limit large molecule movement. [NIH]

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]

Carcinogenesis: The process by which normal cells are transformed into cancer cells. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Carcinogens: Substances that increase the risk of neoplasms in humans or animals. Both genotoxic chemicals, which affect DNA directly, and nongenotoxic chemicals, which induce neoplasms by other mechanism, are included. [NIH]

Carcinoid: A type of tumor usually found in the gastrointestinal system (most often in the

appendix), and sometimes in the lungs or other sites. Carcinoid tumors are usually benign. [NIH]

Carcinoma: Cancer that begins in the skin or in tissues that line or cover internal organs. [NIH]

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

Cardiac arrest: A sudden stop of heart function. [NIH]

Cardiopulmonary: Having to do with the heart and lungs. [NIH]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular disease: Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

Cardiovascular System: The heart and the blood vessels by which blood is pumped and circulated through the body. [NIH]

Carotene: The general name for a group of pigments found in green, yellow, and leafy vegetables, and yellow fruits. The pigments are fat-soluble, unsaturated aliphatic hydrocarbons functioning as provitamins and are converted to vitamin A through enzymatic processes in the intestinal wall. [NIH]

Carrier Proteins: Transport proteins that carry specific substances in the blood or across cell membranes. [NIH]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

Caspase: Enzyme released by the cell at a crucial stage in apoptosis in order to shred all cellular proteins. [NIH]

Cataract: An opacity, partial or complete, of one or both eyes, on or in the lens or capsule, especially an opacity impairing vision or causing blindness. The many kinds of cataract are classified by their morphology (size, shape, location) or etiology (cause and time of occurrence). [EU]

Catechol: A chemical originally isolated from a type of mimosa tree. Catechol is used as an astringent, an antiseptic, and in photography, electroplating, and making other chemicals. It can also be man-made. [NIH]

Cathepsins: A group of lysosomal proteinases or endopeptidases found in aqueous extracts of a variety of animal tissue. They function optimally within an acidic pH range. [NIH]

Catheterization: Use or insertion of a tubular device into a duct, blood vessel, hollow organ, or body cavity for injecting or withdrawing fluids for diagnostic or therapeutic purposes. It differs from intubation in that the tube here is used to restore or maintain patency in obstructions. [NIH]

Cations: Postively charged atoms, radicals or groups of atoms which travel to the cathode or negative pole during electrolysis. [NIH]

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

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [NIH]

Cavernous Sinus: An irregularly shaped venous space in the dura mater at either side of the sphenoid bone. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell Count: A count of the number of cells of a specific kind, usually measured per unit volume of sample. [NIH]

Cell Cycle: The complex series of phenomena, occurring between the end of one cell division and the end of the next, by which cellular material is divided between daughter cells. [NIH]

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

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

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

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

Cell Physiology: Characteristics and physiological processes of cells from cell division to cell death. [NIH]

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

Cell Respiration: The metabolic process of all living cells (animal and plant) in which oxygen is used to provide a source of energy for the cell. [NIH]

Cell 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]

Cell Transplantation: Transference of cells within an individual, between individuals of the same species, or between individuals of different species. [NIH]

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

Centrifugation: A method of separating organelles or large molecules that relies upon differential sedimentation through a preformed density gradient under the influence of a gravitational field generated in a centrifuge. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

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

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

Cervical: Relating to the neck, or to the neck of any organ or structure. Cervical lymph nodes are located in the neck; cervical cancer refers to cancer of the uterine cervix, which is the lower, narrow end (the "neck") of the uterus. [NIH]

Cervix: The lower, narrow end of the uterus that forms a canal between the uterus and vagina. [NIH]

Chaperonins: A class of sequence-related molecular chaperones found in bacteria,

mitochondria, and plastids. Chaperonins are abundant constitutive proteins that increase in amount after stresses such as heat shock, bacterial infection of macrophages, and an increase in the cellular content of unfolded proteins. Bacterial chaperonins are major immunogens in human bacterial infections because of their accumulation during the stress of infection. Two members of this class of chaperones are chaperonin 10 and chaperonin 60. [NIH]

Chemokines: Class of pro-inflammatory cytokines that have the ability to attract and activate leukocytes. They can be divided into at least three structural branches: C (chemokines, C), CC (chemokines, CC), and CXC (chemokines, CXC), according to variations in a shared cysteine motif. [NIH]

Chemoprevention: The use of drugs, vitamins, or other agents to try to reduce the risk of, or delay the development or recurrence of, cancer. [NIH]

Chemopreventive: Natural or synthetic compound used to intervene in the early precancerous stages of carcinogenesis. [NIH]

Chemotactic Factors: Chemical substances that attract or repel cells or organisms. The concept denotes especially those factors released as a result of tissue injury, invasion, or immunologic activity, that attract leukocytes, macrophages, or other cells to the site of infection or insult. [NIH]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Chest wall: The ribs and muscles, bones, and joints that make up the area of the body between the neck and the abdomen. [NIH]

Chlorine: A greenish-yellow, diatomic gas that is a member of the halogen family of elements. It has the atomic symbol Cl, atomic number 17, and atomic weight 70.906. It is a powerful irritant that can cause fatal pulmonary edema. Chlorine is used in manufacturing, as a reagent in synthetic chemistry, for water purification, and in the production of chlorinated lime, which is used in fabric bleaching. [NIH]

Cholecystitis: Inflammation of the gallbladder. [NIH]

Cholestasis: Impairment of biliary flow at any level from the hepatocyte to Vater's ampulla. [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]

Cholinergic: Resembling acetylcholine in pharmacological action; stimulated by or releasing acetylcholine or a related compound. [EU]

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]

Chromosomal: Pertaining to chromosomes. [EU]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

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

Chronic Disease: Disease or ailment of long duration. [NIH]

Chronic Obstructive Pulmonary Disease: Collective term for chronic bronchitis and emphysema. [NIH]

Chronic renal: Slow and progressive loss of kidney function over several years, often resulting in end-stage renal disease. People with end-stage renal disease need dialysis or transplantation to replace the work of the kidneys. [NIH]

Chymopapain: A cysteine endopeptidase isolated from papaya latex. Preferential cleavage at glutamic and aspartic acid residues. EC 3.4.22.6. [NIH]

Chymotrypsin: A serine endopeptidase secreted by the pancreas as its zymogen, chymotrypsinogen and carried in the pancreatic juice to the duodenum where it is activated by trypsin. It selectively cleaves aromatic amino acids on the carboxyl side. [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]

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]

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]

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]

Clot Retraction: Retraction of a clot resulting from contraction of platelet pseudopods attached to fibrin strands that is dependent on the contractile protein thrombosthenin. Used as a measure of platelet function. [NIH]

Coagulation: 1. The process of clot formation. 2. In colloid chemistry, the solidification of a sol into a gelatinous mass; an alteration of a disperse phase or of a dissolved solid which causes the separation of the system into a liquid phase and an insoluble mass called the clot or curd. Coagulation is usually irreversible. 3. In surgery, the disruption of tissue by physical means to form an amorphous residuum, as in electrocoagulation and photocoagulation. [EU]

Coal: A natural fuel formed by partial decomposition of vegetable matter under certain environmental conditions. [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]

Cohort Studies: Studies in which subsets of a defined population are identified. These groups may or may not be exposed to factors hypothesized to influence the probability of the occurrence of a particular disease or other outcome. Cohorts are defined populations which, as a whole, are followed in an attempt to determine distinguishing subgroup characteristics. [NIH]

Colitis: Inflammation of the colon. [NIH]

Collagen: A polypeptide substance comprising about one third of the total protein in

mammalian organisms. It is the main constituent of skin, connective tissue, and the organic substance of bones and teeth. Different forms of collagen are produced in the body but all consist of three alpha-polypeptide chains arranged in a triple helix. Collagen is differentiated from other fibrous proteins, such as elastin, by the content of proline, hydroxyproline, and hydroxylysine; by the absence of tryptophan; and particularly by the high content of polar groups which are responsible for its swelling properties. [NIH]

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

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

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]

Complement 1: The first complement component to act in the cytolysis reaction. It is a trimolecular complex held together with Ca ions and, when activated, has esterase activity which initiates the next step in the sequence. [NIH]

Complement 1 Inactivators: Compounds which inhibit, antagonize, or inactivate complement 1. A well-known inhibitor is a serum glycoprotein believed to be alpha-2-neuroaminoglycoprotein. It inhibits the activated (esterase) form of complement 1 as well as kinin-forming, coagulation, and fibrinolytic systems. Deficiency of this inactivator has been found in patients with hereditary angioneurotic edema. These compounds are members of the serpin superfamily. [NIH]

Complement Activation: The sequential activation of serum components C1 through C9, initiated by an erythrocyte-antibody complex or by microbial polysaccharides and properdin, and producing an inflammatory response. [NIH]

Complementary and alternative medicine: CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy,

spiritual healing, and meditation. [NIH]

Complementary medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used to enhance or complement the standard treatments. Complementary medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

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]

Computerized axial tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called CAT scan, computed tomography (CT scan), or computerized tomography. [NIH]

Computerized tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized axial tomography (CAT) scan and computed tomography (CT scan). [NIH]

Concomitant: Accompanying; accessory; joined with another. [EU]

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

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

Congestion: Excessive or abnormal accumulation of blood in a part. [EU]

Congestive heart failure: Weakness of the heart muscle that leads to a buildup of fluid in body tissues. [NIH]

Conjugated: Acting or operating as if joined; simultaneous. [EU]

Conjugation: 1. The act of joining together or the state of being conjugated. 2. A sexual process seen in bacteria, ciliate protozoa, and certain fungi in which nuclear material is exchanged during the temporary fusion of two cells (conjugants). In bacterial genetics a form of sexual reproduction in which a donor bacterium (male) contributes some, or all, of its DNA (in the form of a replicated set) to a recipient (female) which then incorporates differing genetic information into its own chromosome by recombination and passes the recombined set on to its progeny by replication. In ciliate protozoa, two conjugants of separate mating types exchange micronuclear material and then separate, each now being a fertilized cell. In certain fungi, the process involves fusion of two gametes, resulting in union of their nuclei and formation of a zygote. 3. In chemistry, the joining together of two compounds to produce another compound, such as the combination of a toxic product with some substance in the body to form a detoxified product, which is then eliminated. [EU]

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]

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

Constipation: Infrequent or difficult evacuation of feces. [NIH]

Constriction: The act of constricting. [NIH]

Constriction, Pathologic: The condition of an anatomical structure's being constricted beyond normal dimensions. [NIH]

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]

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]

Control group: In a clinical trial, the group that does not receive the new treatment being studied. This group is compared to the group that receives the new treatment, to see if the new treatment works. [NIH]

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

Conus: A large, circular, white patch around the optic disk due to the exposing of the sclera as a result of degenerative change or congenital abnormality in the choroid and retina. [NIH]

Coordination: Muscular or motor regulation or the harmonious cooperation of muscles or groups of muscles, in a complex action or series of actions. [NIH]

Cornea: The transparent part of the eye that covers the iris and the pupil and allows light to enter the inside. [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 Arteriosclerosis: Thickening and loss of elasticity of the coronary arteries. [NIH]

Coronary heart disease: A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

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

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

Corticosteroids: Hormones that have antitumor activity in lymphomas and lymphoid leukemias; in addition, corticosteroids (steroids) may be used for hormone replacement and for the management of some of the complications of cancer and its treatment. [NIH]

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

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

Creatinine: A compound that is excreted from the body in urine. Creatinine levels are measured to monitor kidney function. [NIH]

Critical Care: Health care provided to a critically ill patient during a medical emergency or crisis. [NIH]

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

Cues: Signals for an action; that specific portion of a perceptual field or pattern of stimuli to which a subject has learned to respond. [NIH]

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

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

Cutaneous: Having to do with the skin. [NIH]

Cyanosis: A bluish or purplish discoloration of the skin and mucous membranes due to an increase in the amount of deoxygenated hemoglobin in the blood or a structural defect in the hemoglobin molecule. [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]

Cycloheximide: Antibiotic substance isolated from streptomycin-producing strains of Streptomyces griseus. It acts by inhibiting elongation during protein synthesis. [NIH]

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

Cysteine: A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

Cystine: A covalently linked dimeric nonessential amino acid formed by the oxidation of cysteine. Two molecules of cysteine are joined together by a disulfide bridge to form cystine. [NIH]

Cystitis: Inflammation of the urinary bladder. [EU]

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]

Cytoprotection: The process by which chemical compounds provide protection to cells against harmful agents. [NIH]

Cytotoxic: Cell-killing. [NIH]

Data Collection: Systematic gathering of data for a particular purpose from various sources, including questionnaires, interviews, observation, existing records, and electronic devices. The process is usually preliminary to statistical analysis of the data. [NIH]

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

Deamination: The removal of an amino group (NH2) from a chemical compound. [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]

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]

Delivery of Health Care: The concept concerned with all aspects of providing and distributing health services to a patient population. [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]

Demyelinating Diseases: Diseases characterized by loss or dysfunction of myelin in the central or peripheral nervous system. [NIH]

Denaturation: Rupture of the hydrogen bonds by heating a DNA solution and then cooling it rapidly causes the two complementary strands to separate. [NIH]

Dendrites: Extensions of the nerve cell body. They are short and branched and receive stimuli from other neurons. [NIH]

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

Dental Care: The total of dental diagnostic, preventive, and restorative services provided to meet the needs of a patient (from Illustrated Dictionary of Dentistry, 1982). [NIH]

Dental 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]

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

Dermatitis: Any inflammation of the skin. [NIH]

Desensitization: The prevention or reduction of immediate hypersensitivity reactions by administration of graded doses of allergen; called also hyposensitization and immunotherapy. [EU]

Desmosine: 4-(4-Amino-4-carboxybutyl)-1-(5-amino-5-carboxypentyl)-3,5-bis(3-amino-3-carboxypropyl)pyridinium. A rare amino acid found in elastin, formed by condensation of four molecules of lysine into a pyridinium ring. [NIH]

Deuterium: Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [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]

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]

Diaphragm: The musculofibrous partition that separates the thoracic cavity from the abdominal cavity. Contraction of the diaphragm increases the volume of the thoracic cavity aiding inspiration. [NIH]

Diarrhoea: Abnormal frequency and liquidity of faecal discharges. [EU]

Diastolic: Of or pertaining to the diastole. [EU]

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]

Diffusivity: Of a reverberant sound field. The degree to which the directions of propagation of waves are random from point to point. [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]

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]

Dilution: A diluted or attenuated medicine; in homeopathy, the diffusion of a given quantity of a medicinal agent in ten or one hundred times the same quantity of water. [NIH]

Diplopia: A visual symptom in which a single object is perceived by the visual cortex as two objects rather than one. Disorders associated with this condition include refractive errors; strabismus; oculomotor nerve diseases; trochlear nerve diseases; abducens nerve diseases; and diseases of the brain stem and occipital lobe. [NIH]

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

Disease Progression: The worsening of a disease over time. This concept is most often used for chronic and incurable diseases where the stage of the disease is an important determinant of therapy and prognosis. [NIH]

Disparity: Failure of the two retinal images of an object to fall on corresponding retinal points. [NIH]

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

Dissociation: 1. The act of separating or state of being separated. 2. The separation of a molecule into two or more fragments (atoms, molecules, ions, or free radicals) produced by the absorption of light or thermal energy or by solvation. 3. In psychology, a defense mechanism in which a group of mental processes are segregated from the rest of a person's mental activity in order to avoid emotional distress, as in the dissociative disorders (q.v.), or

in which an idea or object is segregated from its emotional significance; in the first sense it is roughly equivalent to splitting, in the second, to isolation. 4. A defect of mental integration in which one or more groups of mental processes become separated off from normal consciousness and, thus separated, function as a unitary whole. [EU]

Distal: Remote; farther from any point of reference; opposed to proximal. In dentistry, used to designate a position on the dental arch farther from the median line of the jaw. [EU]

Distention: The state of being distended or enlarged; the act of distending. [EU]

Diuresis: Increased excretion of urine. [EU]

Diuretic: A drug that increases the production of urine. [NIH]

Dolichol: Eicosamethyl octacontanonadecasen-1-o1. Polyprenol found in animal tissues that contains about 20 isoprene residues, the one carrying the alcohol group being saturated. [NIH]

Domesticated: Species in which the evolutionary process has been influenced by humans to meet their needs. [NIH]

Dominance: In genetics, the full phenotypic expression of a gene in both heterozygotes and homozygotes. [EU]

Dorsum: A plate of bone which forms the posterior boundary of the sella turcica. [NIH]

Dose-rate: The strength of a treatment given over a period of time. [NIH]

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

Drug Tolerance: Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

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

Ductus Arteriosus: A fetal blood vessel connecting the pulmonary artery with the descending aorta. [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]

Dysgenesis: Defective development. [EU]

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

Dyspnea: Difficult or labored breathing. [NIH]

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

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

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

Effector: It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

Efficacy: The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomized control trial. [NIH]

Ejection fraction: A measure of ventricular contractility, equal to normally 65 8 per cent; lower values indicate ventricular dysfunction. [EU]

Elasticity: Resistance and recovery from distortion of shape. [NIH]

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

Electric Conductivity: The ability of a substrate to allow the passage of electrons. [NIH]

Electrocardiogram: Measurement of electrical activity during heartbeats. [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]

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]

Electroplating: Coating with a metal or alloy by electrolysis. [NIH]

Emboli: Bit of foreign matter which enters the blood stream at one point and is carried until it is lodged or impacted in an artery and obstructs it. It may be a blood clot, an air bubble, fat or other tissue, or clumps of bacteria. [NIH]

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]

Emollient: Softening or soothing; called also malactic. [EU]

Emphysema: A pathological accumulation of air in tissues or organs. [NIH]

Emulsion: A preparation of one liquid distributed in small globules throughout the body of a second liquid. The dispersed liquid is the discontinuous phase, and the dispersion medium is the continuous phase. When oil is the dispersed liquid and an aqueous solution is the continuous phase, it is known as an oil-in-water emulsion, whereas when water or aqueous solution is the dispersed phase and oil or oleaginous substance is the continuous phase, it is known as a water-in-oil emulsion. Pharmaceutical emulsions for which official standards have been promulgated include cod liver oil emulsion, cod liver oil emulsion with malt, liquid petrolatum emulsion, and phenolphthalein in liquid petrolatum emulsion. [EU]

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

Encephalitis: Inflammation of the brain due to infection, autoimmune processes, toxins, and other conditions. Viral infections (see encephalitis, viral) are a relatively frequent cause of this condition. [NIH]

Encephalitis, Viral: Inflammation of brain parenchymal tissue as a result of viral infection. Encephalitis may occur as primary or secondary manifestation of Togaviridae infections; Herpesviridae infections; Adenoviridae infections; Flaviviridae infections; Bunyaviridae infections; Picornaviridae infections; Paramyxoviridae infections; Orthomyxoviridae infections; Retroviridae infections; and Arenaviridae infections. [NIH]

Endarterectomy: Surgical excision, performed under general anesthesia, of the atheromatous tunica intima of an artery. When reconstruction of an artery is performed as an endovascular procedure through a catheter, it is called atherectomy. [NIH]

Endocrine System: The system of glands that release their secretions (hormones) directly into the circulatory system. In addition to the endocrine glands, included are the chromaffin system and the neurosecretory systems. [NIH]

Endocytosis: Cellular uptake of extracellular materials within membrane-limited vacuoles or microvesicles. Endosomes play a central role in endocytosis. [NIH]

Endodontics: A dental specialty concerned with the maintenance of the dental pulp in a state of health and the treatment of the pulp cavity (pulp chamber and pulp canal). [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]

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

Endoscopic: A technique where a lateral-view endoscope is passed orally to the duodenum for visualization of the ampulla of Vater. [NIH]

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]

Endotoxemia: A condition characterized by the presence of endotoxins in the blood. If endotoxemia is the result of gram-negative rod-shaped bacteria, shock may occur. [NIH]

Endotoxic: Of, relating to, or acting as an endotoxin (= a heat-stable toxin, associated with the outer membranes of certain gram-negative bacteria. Endotoxins are not secreted and are released only when the cells are disrupted). [EU]

Endotoxin: Toxin from cell walls of bacteria. [NIH]

End-stage renal: Total chronic kidney failure. When the kidneys fail, the body retains fluid and harmful wastes build up. A person with ESRD needs treatment to replace the work of the failed kidneys. [NIH]

Enhancer: Transcriptional element in the virus genome. [NIH]

Enteral Nutrition: Nutritional support given via the alimentary canal or any route connected to the gastrointestinal system (i.e., the enteral route). This includes oral feeding, sip feeding, and tube feeding using nasogastric, gastrostomy, and jejunostomy tubes. [NIH]

Enteropeptidase: A specialized proteolytic enzyme secreted by intestinal cells. It converts trypsinogen into its active form trypsin by removing the N-terminal peptide. EC 3.4.21.9. [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]

Environmental Pollutants: Substances which pollute the environment. Use for environmental pollutants in general or for which there is no specific heading. [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]

Eosinophil: A polymorphonuclear leucocyte with large eosinophilic granules in its cytoplasm, which plays a role in hypersensitivity reactions. [NIH]

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

Eosinophilic: A condition found primarily in grinding workers caused by a reaction of the pulmonary tissue, in particular the eosinophilic cells, to dust that has entered the lung. [NIH]

Ephemeral Fever: An Ephemerovirus infection of cattle caused by bovine ephemeral fever virus (ephemeral fever virus, bovine). It is characterized by respiratory symptoms, increased oropharyngeal secretions and lacrimation, joint pains, tremor, and stiffness. [NIH]

Ephemeral Fever Virus, Bovine: The type species of Ephemerovirus causing disease in cattle. Transmission is by hematophagous arthropods and the virus has been isolated from both culicoides and mosquitoes. [NIH]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epidermal: Pertaining to or resembling epidermis. Called also epidermic or epidermoid. [EU]

Epidermal Growth Factor: A 6 kD polypeptide growth factor initially discovered in mouse submaxillary glands. Human epidermal growth factor was originally isolated from urine based on its ability to inhibit gastric secretion and called urogastrone. epidermal growth factor exerts a wide variety of biological effects including the promotion of proliferation and differentiation of mesenchymal and epithelial cells. [NIH]

Epidermis: Nonvascular layer of the skin. It is made up, from within outward, of five layers: 1) basal layer (stratum basale epidermidis); 2) spinous layer (stratum spinosum epidermidis); 3) granular layer (stratum granulosum epidermidis); 4) clear layer (stratum lucidum epidermidis); and 5) horny layer (stratum corneum epidermidis). [NIH]

Epidural: The space between the wall of the spinal canal and the covering of the spinal cord. An epidural injection is given into this space. [NIH]

Epigastric: Having to do with the upper middle area of the abdomen. [NIH]

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

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]

Erythrocyte Volume: Volume of circulating erythrocytes. It is usually measured by radioisotope dilution technique. [NIH]

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

Esophageal: Having to do with the esophagus, the muscular tube through which food passes from the throat to the stomach. [NIH]

Esophagitis: Inflammation, acute or chronic, of the esophagus caused by bacteria, chemicals, or trauma. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Essential Tremor: A rhythmic, involuntary, purposeless, oscillating movement resulting from the alternate contraction and relaxation of opposing groups of muscles. [NIH]

Ethanol: A clear, colorless liquid rapidly absorbed from the gastrointestinal tract and distributed throughout the body. It has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations as well as serving as the primary ingredient in alcoholic beverages. [NIH]

Ethmoid: An unpaired cranial bone which helps form the medial walls of the orbits and contains the themoidal air cells which drain into the nose. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Evacuation: An emptying, as of the bowels. [EU]

Evoke: The electric response recorded from the cerebral cortex after stimulation of a peripheral sense organ. [NIH]

Excrete: To get rid of waste from the body. [NIH]

Exercise Test: Controlled physical activity, more strenuous than at rest, which is performed in order to allow assessment of physiological functions, particularly cardiovascular and pulmonary, but also aerobic capacity. Maximal (most intense) exercise is usually required but submaximal exercise is also used. The intensity of exercise is often graded, using criteria such as rate of work done, oxygen consumption, and heart rate. Physiological data obtained from an exercise test may be used for diagnosis, prognosis, and evaluation of disease severity, and to evaluate therapy. Data may also be used in prescribing exercise by determining a person's exercise capacity. [NIH]

Exercise Tolerance: The exercise capacity of an individual as measured by endurance (maximal exercise duration and/or maximal attained work load) during an exercise test. [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]

Expiration: The act of breathing out, or expelling air from the lungs. [EU]

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

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

External-beam radiation: Radiation therapy that uses a machine to aim high-energy rays at the cancer. Also called external radiation. [NIH]

Extracellular: Outside a cell or cells. [EU]

Extracellular Matrix: A meshwork-like substance found within the extracellular space and in association with the basement membrane of the cell surface. It promotes cellular proliferation and provides a supporting structure to which cells or cell lysates in culture dishes adhere. [NIH]

Extracellular 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]

Extravasation: A discharge or escape, as of blood, from a vessel into the tissues. [EU]

Failure to Thrive: A condition in which an infant or child's weight gain and growth are far below usual levels for age. [NIH]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Fasciitis: Inflammation of the fascia. There are three major types: 1) Eosinophilic fasciitis, an inflammatory reaction with eosinophilia, producing hard thickened skin with an orange-peel configuration suggestive of scleroderma and considered by some a variant of scleroderma; 2) Necrotizing fasciitis, a serious fulminating infection (usually by a beta hemolytic Streptococcus) causing extensive necrosis of superficial fascia; 3) Nodular/Pseudosarcomatous/Proliferative fasciitis, characterized by a rapid growth of fibroblasts with mononuclear inflammatory cells and proliferating capillaries in soft tissue, often the forearm; it is not malignant but is sometimes mistaken for fibrosarcoma. [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]

Feasibility Studies: Studies to determine the advantages or disadvantages, practicability, or

capability of accomplishing a projected plan, study, or project. [NIH]

Feces: The excrement discharged from the intestines, consisting of bacteria, cells exfoliated from the intestines, secretions, chiefly of the liver, and a small amount of food residue. [EU]

Femoral: Pertaining to the femur, or to the thigh. [EU]

Femur: The longest and largest bone of the skeleton, it is situated between the hip and the knee. [NIH]

Fermentation: An enzyme-induced chemical change in organic compounds that takes place in the absence of oxygen. The change usually results in the production of ethanol or lactic acid, and the production of energy. [NIH]

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

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

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]

Fibrinolysis: The natural enzymatic dissolution of fibrin. [NIH]

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

Fibronectin: An adhesive glycoprotein. One form circulates in plasma, acting as an opsonin; another is a cell-surface protein which mediates cellular adhesive interactions. [NIH]

Fibrosarcoma: A type of soft tissue sarcoma that begins in fibrous tissue, which holds bones, muscles, and other organs in place. [NIH]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

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

Fixation: 1. The act or operation of holding, suturing, or fastening in a fixed position. 2. The condition of being held in a fixed position. 3. In psychiatry, a term with two related but distinct meanings : (1) arrest of development at a particular stage, which like regression (return to an earlier stage), if temporary is a normal reaction to setbacks and difficulties but if protracted or frequent is a cause of developmental failures and emotional problems, and (2) a close and suffocating attachment to another person, especially a childhood figure, such as one's mother or father. Both meanings are derived from psychoanalytic theory and refer to 'fixation' of libidinal energy either in a specific erogenous zone, hence fixation at the oral, anal, or phallic stage, or in a specific object, hence mother or father fixation. 4. The use of a fixative (q.v.) to preserve histological or cytological specimens. 5. In chemistry, the process whereby a substance is removed from the gaseous or solution phase and localized, as in carbon dioxide fixation or nitrogen fixation. 6. In ophthalmology, direction of the gaze so that the visual image of the object falls on the fovea centralis. 7. In film processing, the

chemical removal of all undeveloped salts of the film emulsion, leaving only the developed silver to form a permanent image. [EU]

Flatus: Gas passed through the rectum. [NIH]

Flexion: In gynaecology, a displacement of the uterus in which the organ is bent so far forward or backward that an acute angle forms between the fundus and the cervix. [EU]

Fold: A plication or doubling of various parts of the body. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Fossa: A cavity, depression, or pit. [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]

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]

Furosemide: A sulfamyl saluretic and diuretic. It has a fast onset and short duration of action and is used in edema and chronic renal insufficiency. [NIH]

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]

Gamma Rays: Very powerful and penetrating, high-energy electromagnetic radiation of shorter wavelength than that of x-rays. They are emitted by a decaying nucleus, usually between 0.01 and 10 MeV. They are also called nuclear x-rays. [NIH]

Gamma-interferon: Interferon produced by T-lymphocytes in response to various mitogens and antigens. Gamma interferon appears to have potent antineoplastic, immunoregulatory and antiviral activity. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Ganglion: 1. A knot, or knotlike mass. 2. A general term for a group of nerve cell bodies located outside the central nervous system; occasionally applied to certain nuclear groups within the brain or spinal cord, e.g. basal ganglia. 3. A benign cystic tumour occurring on a aponeurosis or tendon, as in the wrist or dorsum of the foot; it consists of a thin fibrous capsule enclosing a clear mucinous fluid. [EU]

Gap Junctions: Connections between cells which allow passage of small molecules and electric current. Gap junctions were first described anatomically as regions of close apposition between cells with a narrow (1-2 nm) gap between cell membranes. The variety in the properties of gap junctions is reflected in the number of connexins, the family of proteins which form the junctions. [NIH]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gas exchange: Primary function of the lungs; transfer of oxygen from inhaled air into the blood and of carbon dioxide from the blood into the lungs. [NIH]

Gas Gangrene: A severe condition resulting from bacteria invading healthy muscle from adjacent traumatized muscle or soft tissue. The infection originates in a wound contaminated with bacteria of the genus Clostridium. C. perfringens accounts for the majority of cases (over eighty percent), while C. noyvi, C. septicum, and C. histolyticum cause most of the other cases. [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastric banding: Surgery to limit the amount of food the stomach can hold by closing part of it off. A band made of special material is placed around the stomach near its upper end, creating a small pouch and a narrow passage into the larger remainder of the stomach. The small outlet delays the emptying of food from the pouch and causes a feeling of fullness. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gastritis: Inflammation of the stomach. [EU]

Gastroesophageal Reflux: Reflux of gastric juice and/or duodenal contents (bile acids, pancreatic juice) into the distal esophagus, commonly due to incompetence of the lower esophageal sphincter. Gastric regurgitation is an extension of this process with entry of fluid into the pharynx or mouth. [NIH]

Gastroesophageal Reflux Disease: Flow of the stomach's contents back up into the esophagus. Happens when the muscle between the esophagus and the stomach (the lower esophageal sphincter) is weak or relaxes when it shouldn't. May cause esophagitis. Also called esophageal reflux or reflux esophagitis. [NIH]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrostomy: Creation of an artificial external opening into the stomach for nutritional support or gastrointestinal compression. [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 Deletion: A genetic rearrangement through loss of segments of DNA or RNA, bringing sequences which are normally separated into close proximity. This deletion may be detected using cytogenetic techniques and can also be inferred from the phenotype, indicating a deletion at one specific locus. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Gene Targeting: The integration of exogenous DNA into the genome of an organism at sites where its expression can be suitably controlled. This integration occurs as a result of homologous recombination. [NIH]

Genetic Code: The specifications for how information, stored in nucleic acid sequence (base sequence), is translated into protein sequence (amino acid sequence). The start, stop, and order of amino acids of a protein is specified by consecutive triplets of nucleotides called codons (codon). [NIH]

Genetic Engineering: Directed modification of the gene complement of a living organism by such techniques as altering the DNA, substituting genetic material by means of a virus, transplanting whole nuclei, transplanting cell hybrids, etc. [NIH]

Genetic Markers: A phenotypically recognizable genetic trait which can be used to identify a genetic locus, a linkage group, or a recombination event. [NIH]

Genetic testing: Analyzing DNA to look for a genetic alteration that may indicate an

increased risk for developing a specific disease or disorder. [NIH]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Gestation: The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

Gestational: Psychosis attributable to or occurring during pregnancy. [NIH]

Gestational Age: Age of the conceptus. In humans, this may be assessed by medical history, physical examination, early immunologic pregnancy tests, radiography, ultrasonography, and amniotic fluid analysis. [NIH]

Giant Cells: Multinucleated masses produced by the fusion of many cells; often associated with viral infections. In AIDS, they are induced when the envelope glycoprotein of the HIV virus binds to the CD4 antigen of uninfected neighboring T4 cells. The resulting syncytium leads to cell death and thus may account for the cytopathic effect of the virus. [NIH]

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]

Glioma: A cancer of the brain that comes from glial, or supportive, cells. [NIH]

Glomerular: Pertaining to or of the nature of a glomerulus, especially a renal glomerulus. [EU]

Glomeruli: Plural of glomerulus. [NIH]

Glomerulonephritis: Glomerular disease characterized by an inflammatory reaction, with leukocyte infiltration and cellular proliferation of the glomeruli, or that appears to be the result of immune glomerular injury. [NIH]

Glucocorticoid: A compound that belongs to the family of compounds called corticosteroids (steroids). Glucocorticoids affect metabolism and have anti-inflammatory and immunosuppressive effects. They may be naturally produced (hormones) or synthetic (drugs). [NIH]

Glucose: D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

Glucose Intolerance: A pathological state in which the fasting plasma glucose level is less than 140 mg per deciliter and the 30-, 60-, or 90-minute plasma glucose concentration following a glucose tolerance test exceeds 200 mg per deciliter. This condition is seen frequently in diabetes mellitus but also occurs with other diseases. [NIH]

Glucuronic Acid: Derivatives of uronic acid found throughout the plant and animal kingdoms. They detoxify drugs and toxins by conjugating with them to form glucuronides in the liver which are more water-soluble metabolites that can be easily eliminated from the body. [NIH]

Glutamate: Excitatory neurotransmitter of the brain. [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]

Glycols: A generic grouping for dihydric alcohols with the hydroxy groups (-OH) located on different carbon atoms. They are viscous liquids with high boiling points for their molecular weights. [NIH]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Glycosaminoglycans: Heteropolysaccharides which contain an N-acetylated hexosamine in a characteristic repeating disaccharide unit. The repeating structure of each disaccharide involves alternate 1,4- and 1,3-linkages consisting of either N-acetylglucosamine or N-acetylgalactosamine. [NIH]

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]

Gout: Hereditary metabolic disorder characterized by recurrent acute arthritis, hyperuricemia and deposition of sodium urate in and around the joints, sometimes with formation of uric acid calculi. [NIH]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

Grading: A system for classifying cancer cells in terms of how abnormal they appear when examined under a microscope. The objective of a grading system is to provide information about the probable growth rate of the tumor and its tendency to spread. The systems used to grade tumors vary with each type of cancer. Grading plays a role in treatment decisions. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

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]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Groin: The external junctural region between the lower part of the abdomen and the thigh. [NIH]

Growth: The progressive development of a living being or part of an organism from its earliest stage to maturity. [NIH]

Growth factors: Substances made by the body that function to regulate cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy. [NIH]

Guanylate Cyclase: An enzyme that catalyzes the conversion of GTP to 3',5'-cyclic GMP and pyrophosphate. It also acts on ITP and dGTP. (From Enzyme Nomenclature, 1992) EC 4.6.1.2. [NIH]

Guinea Pigs: A common name used for the family Caviidae. The most common species is Cavia porcellus which is the domesticated guinea pig used for pets and biomedical research. [NIH]

Habitual: Of the nature of a habit; according to habit; established by or repeated by force of habit, customary. [EU]

Haematoma: A localized collection of blood, usually clotted, in an organ, space, or tissue, due to a break in the wall of a blood vessel. [EU]

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]

Haplotypes: The genetic constitution of individuals with respect to one member of a pair of allelic genes, or sets of genes that are closely linked and tend to be inherited together such as those of the major histocompatibility complex. [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]

Health Care Costs: The actual costs of providing services related to the delivery of health care, including the costs of procedures, therapies, and medications. It is differentiated from health expenditures, which refers to the amount of money paid for the services, and from fees, which refers to the amount charged, regardless of cost. [NIH]

Health Expenditures: The amounts spent by individuals, groups, nations, or private or public organizations for total health care and/or its various components. These amounts may or may not be equivalent to the actual costs (health care costs) and may or may not be shared among the patient, insurers, and/or employers. [NIH]

Health Services: Services for the diagnosis and treatment of disease and the maintenance of health. [NIH]

Health Status: The level of health of the individual, group, or population as subjectively assessed by the individual or by more objective measures. [NIH]

Healthy Worker Effect: Phenomenon of workers' usually exhibiting overall death rates lower than those of the general population due to the fact that the severely ill and disabled are ordinarily excluded from employment. [NIH]

Heart attack: A seizure of weak or abnormal functioning of the heart. [NIH]

Heart failure: Loss of pumping ability by the heart, often accompanied by fatigue, breathlessness, and excess fluid accumulation in body tissues. [NIH]

Heat-Shock Proteins: Proteins which are synthesized in eukaryotic organisms and bacteria in response to hyperthermia and other environmental stresses. They increase thermal tolerance and perform functions essential to cell survival under these conditions. [NIH]

Heat-Shock Proteins 90: A class of molecular chaperones whose members act in the mechanism of signal transduction by steroid receptors. [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]

Hemodialysis: The use of a machine to clean wastes from the blood after the kidneys have failed. The blood travels through tubes to a dialyzer, which removes wastes and extra fluid. The cleaned blood then flows through another set of tubes back into the body. [NIH]

Hemodynamics: The movements of the blood and the forces involved in systemic or regional blood circulation. [NIH]

Hemoglobin: One of the fractions of glycosylated hemoglobin A1c. Glycosylated hemoglobin is formed when linkages of glucose and related monosaccharides bind to hemoglobin A and its concentration represents the average blood glucose level over the previous several weeks. HbA1c levels are used as a measure of long-term control of plasma glucose (normal, 4 to 6 percent). In controlled diabetes mellitus, the concentration of glycosylated hemoglobin A is within the normal range, but in uncontrolled cases the level may be 3 to 4 times the normal conentration. Generally, complications are substantially lower among patients with Hb levels of 7 percent or less than in patients with HbA1c levels of 9 percent or more. [NIH]

Hemoglobinuria: The presence of free hemoglobin in the urine. [NIH]

Hemolytic: A disease that affects the blood and blood vessels. It destroys red blood cells, cells that cause the blood to clot, and the lining of blood vessels. HUS is often caused by the Escherichia coli bacterium in contaminated food. People with HUS may develop acute renal failure. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Heparan Sulfate Proteoglycan: A substance released by astrocytes, which is critical in stopping nervous fibers in their tracks. [NIH]

Heparin: Heparinic acid. A highly acidic mucopolysaccharide formed of equal parts of sulfated D-glucosamine and D-glucuronic acid with sulfaminic bridges. The molecular weight ranges from six to twenty thousand. Heparin occurs in and is obtained from liver, lung, mast cells, etc., of vertebrates. Its function is unknown, but it is used to prevent blood clotting in vivo and vitro, in the form of many different salts. [NIH]

Hepatic: Refers to the liver. [NIH]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatocellular: Pertaining to or affecting liver cells. [EU]

Hepatocellular carcinoma: A type of adenocarcinoma, the most common type of liver tumor. [NIH]

Hepatocyte: A liver cell. [NIH]

Hepatoma: A liver tumor. [NIH]

Hepatotoxic: Toxic to liver cells. [EU]

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]

Hernia: Protrusion of a loop or knuckle of an organ or tissue through an abnormal opening. [NIH]

Herniorrhaphy: An operation to repair a hernia. [NIH]

Heterodimer: Zippered pair of nonidentical proteins. [NIH]

Heterogeneity: The property of one or more samples or populations which implies that they are not identical in respect of some or all of their parameters, e. g. heterogeneity of variance. [NIH]

Heterozygotes: Having unlike alleles at one or more corresponding loci on homologous chromosomes. [NIH]

Histology: The study of tissues and cells under a microscope. [NIH]

Hoarseness: An unnaturally deep or rough quality of voice. [NIH]

Holidays: Days commemorating events. Holidays also include vacation periods. [NIH]

Homeostasis: The processes whereby the internal environment of an organism tends to remain balanced and stable. [NIH]

Homogeneous: Consisting of or composed of similar elements or ingredients; of a uniform quality throughout. [EU]

Homologous: Corresponding in structure, position, origin, etc., as (a) the feathers of a bird and the scales of a fish, (b) antigen and its specific antibody, (c) allelic chromosomes. [EU]

Homozygotes: An individual having a homozygous gene pair. [NIH]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Hormone therapy: Treatment of cancer by removing, blocking, or adding hormones. Also called endocrine therapy. [NIH]

Host: Any animal that receives a transplanted graft. [NIH]

Housekeeping: The care and management of property. [NIH]

Humoral: Of, relating to, proceeding from, or involving a bodily humour - now often used of endocrine factors as opposed to neural or somatic. [EU]

Humour: 1. A normal functioning fluid or semifluid of the body (as the blood, lymph or bile) especially of vertebrates. 2. A secretion that is itself an excitant of activity (as certain hormones). [EU]

Hyaline membrane disease: A respiratory disease of newborns, especially premature infants, in which a membrane composed of proteins and dead cells forms and lines the alveoli making gas exchange difficult or impossible. [NIH]

Hyaluronidase: An enzyme that splits hyaluronic acid and thus lowers the viscosity of the acid and facilitates the spreading of fluids through tissues either advantageously or disadvantageously. [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]

Hydrogen: The first chemical element in the periodic table. It has the atomic symbol H, atomic number 1, and atomic weight 1. It exists, under normal conditions, as a colorless,

odorless, tasteless, diatomic gas. Hydrogen ions are protons. Besides the common H1 isotope, hydrogen exists as the stable isotope deuterium and the unstable, radioactive isotope tritium. [NIH]

Hydrogen Peroxide: A strong oxidizing agent used in aqueous solution as a ripening agent, bleach, and topical anti-infective. It is relatively unstable and solutions deteriorate over time unless stabilized by the addition of acetanilide or similar organic materials. [NIH]

Hydrolysis: The process of cleaving a chemical compound by the addition of a molecule of water. [NIH]

Hydrophobic: Not readily absorbing water, or being adversely affected by water, as a hydrophobic colloid. [EU]

Hydroxides: Inorganic compounds that contain the OH- group. [NIH]

Hydroxyl Radical: The univalent radical OH that is present in hydroxides, alcohols, phenols, glycols. [NIH]

Hydroxylysine: A hydroxylated derivative of the amino acid lysine that is present in certain collagens. [NIH]

Hydroxyproline: A hydroxylated form of the imino acid proline. A deficiency in ascorbic acid can result in impaired hydroxyproline formation. [NIH]

Hyperbaric: Characterized by greater than normal pressure or weight; applied to gases under greater than atmospheric pressure, as hyperbaric oxygen, or to a solution of greater specific gravity than another taken as a standard of reference. [EU]

Hyperbaric oxygen: Oxygen that is at an atmospheric pressure higher than the pressure at sea level. Breathing hyperbaric oxygen to enhance the effectiveness of radiation therapy is being studied. [NIH]

Hyperbilirubinemia: Pathologic process consisting of an abnormal increase in the amount of bilirubin in the circulating blood, which may result in jaundice. [NIH]

Hypercalcemia: Abnormally high level of calcium in the blood. [NIH]

Hypercapnia: A clinical manifestation of abnormal increase in the amount of carbon dioxide in arterial blood. [NIH]

Hypercarbia: Excess of carbon dioxide in the blood. [NIH]

Hyperglycemia: Abnormally high blood sugar. [NIH]

Hyperlipidemia: An excess of lipids in the blood. [NIH]

Hyperlipoproteinemia: Metabolic disease characterized by elevated plasma cholesterol and/or triglyceride levels. The inherited form is attributed to a single gene mechanism. [NIH]

Hyperoxia: An abnormal increase in the amount of oxygen in the tissues and organs. [NIH]

Hyperplasia: An increase in the number of cells in a tissue or organ, not due to tumor formation. It differs from hypertrophy, which is an increase in bulk without an increase in the number of cells. [NIH]

Hyperreactive: Describes a situation in which a body tissue is especially likely to have an exaggerated reaction to a particular situation. [NIH]

Hypersecretion: Excessive secretion. [EU]

Hypersensitivity: Altered reactivity to an antigen, which can result in pathologic reactions upon subsequent exposure to that particular antigen. [NIH]

Hypersensitivity, Immediate: Hypersensitivity reactions which occur within minutes of exposure to challenging antigen due to the release of histamine which follows the antigen-antibody reaction and causes smooth muscle contraction and increased vascular

permeability. [NIH]

Hypertension: Persistently high arterial blood pressure. Currently accepted threshold levels are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [NIH]

Hypertriglyceridemia: Condition of elevated triglyceride concentration in the blood; an inherited form occurs in familial hyperlipoproteinemia IIb and hyperlipoproteinemia type IV. It has been linked to higher risk of heart disease and arteriosclerosis. [NIH]

Hypertrophy: General increase in bulk of a part or organ, not due to tumor formation, nor to an increase in the number of cells. [NIH]

Hyperuricemia: A buildup of uric acid (a byproduct of metabolism) in the blood; a side effect of some anticancer drugs. [NIH]

Hypochlorous Acid: HClO. An oxyacid of chlorine containing monovalent chlorine that acts as an oxidizing or reducing agent. [NIH]

Hypoglycemia: Abnormally low blood sugar [NIH]

Hypoplasia: Incomplete development or underdevelopment of an organ or tissue. [EU]

Hypothalamus: Ventral part of the diencephalon extending from the region of the optic chiasm to the caudal border of the mammillary bodies and forming the inferior and lateral walls of the third ventricle. [NIH]

Hypoxemia: Deficient oxygenation of the blood; hypoxia. [EU]

Hypoxia: Reduction of oxygen supply to tissue below physiological levels despite adequate perfusion of the tissue by blood. [EU]

Iatrogenic: Resulting from the activity of physicians. Originally applied to disorders induced in the patient by autosuggestion based on the physician's examination, manner, or discussion, the term is now applied to any adverse condition in a patient occurring as the result of treatment by a physician or surgeon, especially to infections acquired by the patient during the course of treatment. [EU]

Id: The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Idiopathic: Describes a disease of unknown cause. [NIH]

Ileus: Obstruction of the intestines. [EU]

Iliac Artery: Either of two large arteries originating from the abdominal aorta; they supply blood to the pelvis, abdominal wall and legs. [NIH]

Immersion: The placing of a body or a part thereof into a liquid. [NIH]

Immune Complex Diseases: Group of diseases mediated by the deposition of large soluble complexes of antigen and antibody with resultant damage to tissue. Besides serum sickness and the arthus reaction, evidence supports a pathogenic role for immune complexes in many other systemic immunologic diseases including glomerulonephritis, systemic lupus erythematosus and polyarteritis nodosa. [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]

Immunoblotting: Immunologic methods for isolating and quantitatively measuring immunoreactive substances. When used with immune reagents such as monoclonal antibodies, the process is known generically as western blot analysis (blotting, western). [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]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

Implant radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called [NIH]

In situ: In the natural or normal place; confined to the site of origin without invasion of neighbouring tissues. [EU]

In Situ Hybridization: A technique that localizes specific nucleic acid sequences within intact chromosomes, eukaryotic cells, or bacterial cells through the use of specific nucleic acid-labeled probes. [NIH]

In vitro: In the laboratory (outside the body). The opposite of in vivo (in the body). [NIH]

In vivo: In the body. The opposite of in vitro (outside the body or in the laboratory). [NIH]

Incision: A cut made in the body during surgery. [NIH]

Incompetence: Physical or mental inadequacy or insufficiency. [EU]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Infantile: Pertaining to an infant or to infancy. [EU]

Infarction: A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

Infection: 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local

infection may persist and spread by extension to become an acute, subacute, or chronic clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

Infiltration: The diffusion or accumulation in a tissue or cells of substances not normal to it or in amounts of the normal. Also, the material so accumulated. [EU]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Inflammatory bowel disease: A general term that refers to the inflammation of the colon and rectum. Inflammatory bowel disease includes ulcerative colitis and Crohn's disease. [NIH]

Influenza: An acute viral infection involving the respiratory tract. It is marked by inflammation of the nasal mucosa, the pharynx, and conjunctiva, and by headache and severe, often generalized, myalgia. [NIH]

Ingestion: Taking into the body by mouth [NIH]

Inguinal: Pertaining to the inguen, or groin. [EU]

Inguinal Hernia: A small part of the large or small intestine or bladder that pushes into the groin. May cause pain and feelings of pressure or burning in the groin. Often requires surgery. [NIH]

Inhalation: The drawing of air or other substances into the lungs. [EU]

Inhalation Exposure: The exposure to potentially harmful chemical, physical, or biological agents by inhaling them. [NIH]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

Inorganic: Pertaining to substances not of organic origin. [EU]

Insight: The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Instillation: . [EU]

Insulator: Material covering the metal conductor of the lead. It is usually polyurethane or silicone. [NIH]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Insulin-dependent diabetes mellitus: A disease characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Autoimmune, genetic, and environmental factors are involved in the development of type I diabetes. [NIH]

Intercostal: Situated between the ribs. [EU]

Interferon: A biological response modifier (a substance that can improve the body's natural response to disease). Interferons interfere with the division of cancer cells and can slow tumor growth. There are several types of interferons, including interferon-alpha, -beta, and -gamma. These substances are normally produced by the body. They are also made in the laboratory for use in treating cancer and other diseases. [NIH]

Interferon-alpha: One of the type I interferons produced by peripheral blood leukocytes or lymphoblastoid cells when exposed to live or inactivated virus, double-stranded RNA, or

bacterial products. It is the major interferon produced by virus-induced leukocyte cultures and, in addition to its pronounced antiviral activity, it causes activation of NK cells. [NIH]

Interleukin-8: A cytokine that activates neutrophils and attracts neutrophils and T-lymphocytes. It is released by several cell types including monocytes, macrophages, T-lymphocytes, fibroblasts, endothelial cells, and keratinocytes by an inflammatory stimulus. IL-8 is a member of the beta-thromboglobulin superfamily and structurally related to platelet factor 4. [NIH]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

Internal Medicine: A medical specialty concerned with the diagnosis and treatment of diseases of the internal organ systems of adults. [NIH]

Internal radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called brachytherapy, implant radiation, or interstitial radiation therapy. [NIH]

Interstitial: Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

Intestinal: Having to do with the intestines. [NIH]

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

Intoxication: Poisoning, the state of being poisoned. [EU]

Intracellular: Inside a cell. [NIH]

Intracranial Pressure: Pressure within the cranial cavity. It is influenced by brain mass, the circulatory system, CSF dynamics, and skull rigidity. [NIH]

Intraocular: Within the eye. [EU]

Intraocular pressure: Pressure of the fluid inside the eye; normal IOP varies among individuals. [NIH]

Intraperitoneal: IP. Within the peritoneal cavity (the area that contains the abdominal organs). [NIH]

Intravenous: IV. Into a vein. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

Introns: Non-coding, intervening sequences of DNA that are transcribed, but are removed from within the primary gene transcript and rapidly degraded during maturation of messenger RNA. Most genes in the nuclei of eukaryotes contain introns, as do mitochondrial and chloroplast genes. [NIH]

Intubation: Introduction of a tube into a hollow organ to restore or maintain patency if obstructed. It is differentiated from catheterization in that the insertion of a catheter is usually performed for the introducing or withdrawing of fluids from the body. [NIH]

Invasive: 1. Having the quality of invasiveness. 2. Involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Involuntary: Reaction occurring without intention or volition. [NIH]

Ion Channels: Gated, ion-selective glycoproteins that traverse membranes. The stimulus for channel gating can be a membrane potential, drug, transmitter, cytoplasmic messenger, or a mechanical deformation. Ion channels which are integral parts of ionotropic neurotransmitter receptors are not included. [NIH]

Ionization: 1. Any process by which a neutral atom gains or loses electrons, thus acquiring a net charge, as the dissociation of a substance in solution into ions or ion production by the

passage of radioactive particles. 2. Iontophoresis. [EU]

Ionizing: Radiation comprising charged particles, e. g. electrons, protons, alpha-particles, etc., having sufficient kinetic energy to produce ionization by collision. [NIH]

Ions: An atom or group of atoms that have a positive or negative electric charge due to a gain (negative charge) or loss (positive charge) of one or more electrons. Atoms with a positive charge are known as cations; those with a negative charge are anions. [NIH]

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]

Irradiation: The use of high-energy radiation from x-rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Irradiation is also called radiation therapy, radiotherapy, and x-ray therapy. [NIH]

Irritants: Drugs that act locally on cutaneous or mucosal surfaces to produce inflammation; those that cause redness due to hyperemia are rubefacients; those that raise blisters are vesicants and those that penetrate sebaceous glands and cause abscesses are pustulants; tear gases and mustard gases are also irritants. [NIH]

Ischemia: Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel. [EU]

Isoleucine: An essential branched-chain amino acid found in many proteins. It is an isomer of LEUCINE. It is important in hemoglobin synthesis and regulation of blood sugar and energy levels. [NIH]

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]

Isozymes: The multiple forms of a single enzyme. [NIH]

Jaundice: A clinical manifestation of hyperbilirubinemia, consisting of deposition of bile pigments in the skin, resulting in a yellowish staining of the skin and mucous membranes. [NIH]

Jejunostomy: Surgical formation of an opening through the abdominal wall into the jejunum, usually for enteral hyperalimentation. [NIH]

Joint: The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

Kallidin: A decapeptide bradykinin homolog produced by the action of tissue and glandular kallikreins on low-molecular-weight kininogen. It is a smooth-muscle stimulant and hypotensive agent that functions through vasodilatation. [NIH]

Kb: A measure of the length of DNA fragments, 1 Kb = 1000 base pairs. The largest DNA fragments are up to 50 kilobases long. [NIH]

Keratinocyte growth factor: A substance that stimulates the growth of epithelial cells that line the surface of the mouth and intestinal tract. [NIH]

Keratinocytes: Epidermal cells which synthesize keratin and undergo characteristic changes as they move upward from the basal layers of the epidermis to the cornified (horny) layer of the skin. Successive stages of differentiation of the keratinocytes forming the epidermal

layers are basal cell, spinous or prickle cell, and the granular cell. [NIH]

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]

Kidney Cortex: The outer zone of the kidney, beneath the capsule, consisting of kidney glomerulus; kidney tubules, distal; and kidney tubules, proximal. [NIH]

Kidney Disease: Any one of several chronic conditions that are caused by damage to the cells of the kidney. People who have had diabetes for a long time may have kidney damage. Also called nephropathy. [NIH]

Kidney Failure: The inability of a kidney to excrete metabolites at normal plasma levels under conditions of normal loading, or the inability to retain electrolytes under conditions of normal intake. In the acute form (kidney failure, acute), it is marked by uremia and usually by oliguria or anuria, with hyperkalemia and pulmonary edema. The chronic form (kidney failure, chronic) is irreversible and requires hemodialysis. [NIH]

Kidney Failure, Acute: A clinical syndrome characterized by a sudden decrease in glomerular filtration rate, often to values of less than 1 to 2 ml per minute. It is usually associated with oliguria (urine volumes of less than 400 ml per day) and is always associated with biochemical consequences of the reduction in glomerular filtration rate such as a rise in blood urea nitrogen (BUN) and serum creatinine concentrations. [NIH]

Kidney Failure, Chronic: An irreversible and usually progressive reduction in renal function in which both kidneys have been damaged by a variety of diseases to the extent that they are unable to adequately remove the metabolic products from the blood and regulate the body's electrolyte composition and acid-base balance. Chronic kidney failure requires hemodialysis or surgery, usually kidney transplantation. [NIH]

Kidney Pelvis: The flattened, funnel-shaped expansion connecting the ureter to the kidney calices. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Labile: 1. Gliding; moving from point to point over the surface; unstable; fluctuating. 2. Chemically unstable. [EU]

Laceration: 1. The act of tearing. 2. A torn, ragged, mangled wound. [EU]

Lactation: The period of the secretion of milk. [EU]

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]

Laryngitis: Inflammation of the larynx. This condition presents itself with dryness and soreness of the throat, difficulty in swallowing, cough, and hoarseness. [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]

Latency: The period of apparent inactivity between the time when a stimulus is presented and the moment a response occurs. [NIH]

Latent: Phoria which occurs at one distance or another and which usually has no troublesome effect. [NIH]

Lavage: A cleaning of the stomach and colon. Uses a special drink and enemas. [NIH]

Laxative: An agent that acts to promote evacuation of the bowel; a cathartic or purgative. [EU]

Lectin: A complex molecule that has both protein and sugars. Lectins are able to bind to the outside of a cell and cause biochemical changes in it. Lectins are made by both animals and plants. [NIH]

Legionella: Gram-negative aerobic rods, isolated from surface water, mud, or thermally polluted lakes or streams. It is pathogenic for man and it has no known soil or animal sources. [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]

Leucocyte: All the white cells of the blood and their precursors (myeloid cell series, lymphoid cell series) but commonly used to indicate granulocytes exclusive of lymphocytes. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Leukocyte Elastase: An enzyme that catalyzes the hydrolysis of proteins, including elastin. It cleaves preferentially bonds at the carboxyl side of Ala and Val, with greater specificity for Ala. EC 3.4.21.37. [NIH]

Leukocytes: White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

Library Services: Services offered to the library user. They include reference and circulation. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and strengthen joints. [EU]

Ligands: A RNA simulation method developed by the MIT. [NIH]

Ligation: Application of a ligature to tie a vessel or strangulate a part. [NIH]

Linear Models: Statistical models in which the value of a parameter for a given value of a factor is assumed to be equal to a + bx, where a and b are constants. The models predict a linear regression. [NIH]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Linkage Disequilibrium: Nonrandom association of linked genes. This is the tendency of the alleles of two separate but already linked loci to be found together more frequently than would be expected by chance alone. [NIH]

Lipid: Fat. [NIH]

Lipid Peroxidation: Peroxidase catalyzed oxidation of lipids using hydrogen peroxide as an electron acceptor. [NIH]

Lipodystrophy: A collection of rare conditions resulting from defective fat metabolism and characterized by atrophy of the subcutaneous fat. They include total, congenital or acquired, partial, abdominal infantile, and localized lipodystrophy. [NIH]

Lipopolysaccharide: Substance consisting of polysaccaride and lipid. [NIH]

Liposome: A spherical particle in an aqueous medium, formed by a lipid bilayer enclosing an aqueous compartment. [EU]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

Liver cancer: A disease in which malignant (cancer) cells are found in the tissues of the liver. [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]

Liver Transplantation: The transference of a part of or an entire liver from one human or animal to another. [NIH]

Lobe: A portion of an organ such as the liver, lung, breast, or brain. [NIH]

Lobectomy: The removal of a lobe. [NIH]

Localization: The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

Localized: Cancer which has not metastasized yet. [NIH]

Longitudinal Studies: Studies in which variables relating to an individual or group of individuals are assessed over a period of time. [NIH]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

Loop: A wire usually of platinum bent at one end into a small loop (usually 4 mm inside diameter) and used in transferring microorganisms. [NIH]

Lower Esophageal Sphincter: The muscle between the esophagus and stomach. When a person swallows, this muscle relaxes to let food pass from the esophagus to the stomach. It stays closed at other times to keep stomach contents from flowing back into the esophagus. [NIH]

Lumen: The cavity or channel within a tube or tubular organ. [EU]

Lung Transplantation: The transference of either one or both of the lungs from one human or animal to another. [NIH]

Lung volume: The amount of air the lungs hold. [NIH]

Lupus: A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

Lymph: The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

Lymph node: A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Also known as a lymph gland. Lymph nodes are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic fluid (lymph). [NIH]

Lymphatic: The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen,

thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphoma: A general term for various neoplastic diseases of the lymphoid tissue. [NIH]

Lysine: An essential amino acid. It is often added to animal feed. [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]

Major Histocompatibility Complex: The genetic region which contains the loci of genes which determine the structure of the serologically defined (SD) and lymphocyte-defined (LD) transplantation antigens, genes which control the structure of the immune response-associated (Ia) antigens, the immune response (Ir) genes which control the ability of an animal to respond immunologically to antigenic stimuli, and genes which determine the structure and/or level of the first four components of complement. [NIH]

Malabsorption: Impaired intestinal absorption of nutrients. [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]

Malnutrition: A condition caused by not eating enough food or not eating a balanced diet. [NIH]

Mammogram: An x-ray of the breast. [NIH]

Mandible: The largest and strongest bone of the face constituting the lower jaw. It supports the lower teeth. [NIH]

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]

Mannosidases: Alpha or beta-Mannoside mannohydrolases. Catalyzes the hydrolysis of terminal, non-reducing alpha or beta-D-mannose residues in mannosides. Deficiency of the alpha form can cause mannosidosis. [NIH]

Mannosides: Glycosides formed by the reaction of the hydroxyl group on the anomeric carbon atom of mannose with an alcohol to form an acetal. They include both alpha- and beta-mannosides. [NIH]

Mannosidosis: Inborn error of metabolism marked by a defect in alpha-mannosidase activity that results in lysosomal accumulation of mannose-rich substrates. Virtually all patients have psychomotor retardation, facial coarsening, and some degree of dysostosis multiplex. It is thought to be an autosomal recessive disorder. [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]

Mechanical ventilation: Use of a machine called a ventilator or respirator to improve the exchange of air between the lungs and the atmosphere. [NIH]

Mechanoreceptors: Cells specialized to transduce mechanical stimuli and relay that information centrally in the nervous system. Mechanoreceptors include hair cells, which mediate hearing and balance, and the various somatosensory receptors, often with non-neural accessory structures. [NIH]

Meconium: The thick green-to-black mucilaginous material found in the intestines of a full-term fetus. It consists of secretions of the intestinal glands, bile pigments, fatty acids, amniotic fluid, and intrauterine debris. It constitutes the first stools passed by a newborn. [NIH]

Meconium Aspiration: Syndrome caused by sucking of thick meconium into the lungs, usually by term or post-term infants (often small for gestational age) either in utero or with first breath. The resultant small airway obstruction may produce respiratory distress, tachypnea, cyanosis, pneumothorax, and/or pneumomediastinum. [NIH]

Medial: Lying near the midsaggital plane of the body; opposed to lateral. [NIH]

Mediastinal Emphysema: Presence of air in the mediastinal tissues due to leakage of air from the tracheobronchial tree, usually as a result of trauma. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

Medicament: A medicinal substance or agent. [EU]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Meiosis: A special method of cell division, occurring in maturation of the germ cells, by means of which each daughter nucleus receives half the number of chromosomes characteristic of the somatic cells of the species. [NIH]

Melanin: The substance that gives the skin its color. [NIH]

Melanocytes: Epidermal dendritic pigment cells which control long-term morphological color changes by alteration in their number or in the amount of pigment they produce and store in the pigment containing organelles called melanosomes. Melanophores are larger cells which do not exist in mammals. [NIH]

Melanoma: A form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

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]

Meningioma: A type of tumor that occurs in the meninges, the membranes that cover and

protect the brain and spinal cord. Meningiomas usually grow slowly. [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]

Mental Disorders: Psychiatric illness or diseases manifested by breakdowns in the adaptational process expressed primarily as abnormalities of thought, feeling, and behavior producing either distress or impairment of function. [NIH]

Mental Health: The state wherein the person is well adjusted. [NIH]

Mentors: Senior professionals who provide guidance, direction and support to those persons desirous of improvement in academic positions, administrative positions or other career development situations. [NIH]

Mesenchymal: Refers to cells that develop into connective tissue, blood vessels, and lymphatic tissue. [NIH]

Mesenteric: Pertaining to the mesentery : a membranous fold attaching various organs to the body wall. [EU]

Metabolic disorder: A condition in which normal metabolic processes are disrupted, usually because of a missing enzyme. [NIH]

Metallothionein: A low-molecular-weight (approx. 10 kD) protein occurring in the cytoplasm of kidney cortex and liver. It is rich in cysteinyl residues and contains no aromatic amino acids. Metallothionein shows high affinity for bivalent heavy metals. [NIH]

Metaplasia: A condition in which there is a change of one adult cell type to another similar adult cell type. [NIH]

Metastasis: The spread of cancer from one part of the body to another. Tumors formed from cells that have spread are called "secondary tumors" and contain cells that are like those in the original (primary) tumor. The plural is metastases. [NIH]

Metastatic: Having to do with metastasis, which is the spread of cancer from one part of the body to another. [NIH]

Methionine: A sulfur containing essential amino acid that is important in many body functions. It is a chelating agent for heavy metals. [NIH]

MI: Myocardial infarction. Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Microbe: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

Microcalcifications: Tiny deposits of calcium in the breast that cannot be felt but can be detected on a mammogram. A cluster of these very small specks of calcium may indicate that cancer is present. [NIH]

Microcirculation: The vascular network lying between the arterioles and venules; includes capillaries, metarterioles and arteriovenous anastomoses. Also, the flow of blood through this network. [NIH]

Microorganism: An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

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]

Microsomal: Of or pertaining to microsomes : vesicular fragments of endoplasmic reticulum formed after disruption and centrifugation of cells. [EU]

Migration: The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

Milliliter: A measure of volume for a liquid. A milliliter is approximately 950-times smaller than a quart and 30-times smaller than a fluid ounce. A milliliter of liquid and a cubic centimeter (cc) of liquid are the same. [NIH]

Mineral Oil: A mixture of liquid hydrocarbons obtained from petroleum. It is used as laxative, lubricant, ointment base, and emollient. [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]

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]

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 Chaperones: A family of cellular proteins that mediate the correct assembly or disassembly of other polypeptides, and in some cases their assembly into oligomeric structures, but which are not components of those final structures. It is believed that chaperone proteins assist polypeptides to self-assemble by inhibiting alternative assembly pathways that produce nonfunctional structures. Some classes of molecular chaperones are the nucleoplasmins, the chaperonins, the heat-shock proteins 70, and the heat-shock proteins 90. [NIH]

Molecule: A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

Monitor: An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

Monoclonal: An antibody produced by culturing a single type of cell. It therefore consists of a single species of immunoglobulin molecules. [NIH]

Monoclonal antibodies: Laboratory-produced substances that can locate and bind to cancer cells wherever they are in the body. Many monoclonal antibodies are used in cancer

detection or therapy; each one recognizes a different protein on certain cancer cells. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to a tumor. [NIH]

Monocyte: A type of white blood cell. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Morphogenesis: The development of the form of an organ, part of the body, or organism. [NIH]

Morphology: The science of the form and structure of organisms (plants, animals, and other forms of life). [NIH]

Mucilaginous: Pertaining to or secreting mucus. [NIH]

Mucinous: Containing or resembling mucin, the main compound in mucus. [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]

Mucolytic: Destroying or dissolving mucin; an agent that so acts : a mucopolysaccharide or glycoprotein, the chief constituent of mucus. [EU]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Mucositis: A complication of some cancer therapies in which the lining of the digestive system becomes inflamed. Often seen as sores in the mouth. [NIH]

Mucus: The viscous secretion of mucous membranes. It contains mucin, white blood cells, water, inorganic salts, and exfoliated cells. [NIH]

Multiple Organ Failure: A progressive condition usually characterized by combined failure of several organs such as the lungs, liver, kidney, along with some clotting mechanisms, usually postinjury or postoperative. [NIH]

Multiple sclerosis: A disorder of the central nervous system marked by weakness, numbness, a loss of muscle coordination, and problems with vision, speech, and bladder control. Multiple sclerosis is thought to be an autoimmune disease in which the body's immune system destroys myelin. Myelin is a substance that contains both protein and fat (lipid) and serves as a nerve insulator and helps in the transmission of nerve signals. [NIH]

Muscle Fatigue: A state arrived at through prolonged and strong contraction of a muscle. Studies in athletes during prolonged submaximal exercise have shown that muscle fatigue increases in almost direct proportion to the rate of muscle glycogen depletion. Muscle fatigue in short-term maximal exercise is associated with oxygen lack and an increased level of blood and muscle lactic acid, and an accompanying increase in hydrogen-ion concentration in the exercised muscle. [NIH]

Muscle Fibers: Large single cells, either cylindrical or prismatic in shape, that form the basic unit of muscle tissue. They consist of a soft contractile substance enclosed in a tubular sheath. [NIH]

Muscle Relaxation: That phase of a muscle twitch during which a muscle returns to a resting position. [NIH]

Muscle tension: A force in a material tending to produce extension; the state of being stretched. [NIH]

Muscular Atrophy: Derangement in size and number of muscle fibers occurring with aging, reduction in blood supply, or following immobilization, prolonged weightlessness,

malnutrition, and particularly in denervation. [NIH]

Muscular Dystrophies: A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

Mustard Gas: Severe irritant and vesicant of skin, eyes, and lungs. It may cause blindness and lethal lung edema and was formerly used as a war gas. The substance has been proposed as a cytostatic and for treatment of psoriasis. It has been listed as a known carcinogen in the Fourth Annual Report on Carcinogens (NTP-85-002, 1985) (Merck, 11th ed). [NIH]

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]

Myalgia: Pain in a muscle or muscles. [EU]

Mycosis: Any disease caused by a fungus. [EU]

Mycotic: Pertaining to a mycosis; caused by fungi. [EU]

Mydriatic: 1. Dilating the pupil. 2. Any drug that dilates the pupil. [EU]

Myelin: The fatty substance that covers and protects nerves. [NIH]

Myeloid Cells: Cells which include the monocytes and the granulocytes. [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]

Myocardial Ischemia: A disorder of cardiac function caused by insufficient blood flow to the muscle tissue of the heart. The decreased blood flow may be due to narrowing of the coronary arteries (coronary arteriosclerosis), to obstruction by a thrombus (coronary thrombosis), or less commonly, to diffuse narrowing of arterioles and other small vessels within the heart. Severe interruption of the blood supply to the myocardial tissue may result in necrosis of cardiac muscle (myocardial infarction). [NIH]

Myocardial Reperfusion: Generally, restoration of blood supply to heart tissue which is ischemic due to decrease in normal blood supply. The decrease may result from any source including atherosclerotic obstruction, narrowing of the artery, or surgical clamping. Reperfusion can be induced to treat ischemia. Methods include chemical dissolution of an occluding thrombus, administration of vasodilator drugs, angioplasty, catheterization, and artery bypass graft surgery. However, it is thought that reperfusion can itself further damage the ischemic tissue, causing myocardial reperfusion injury. [NIH]

Myocardial Reperfusion Injury: Functional, metabolic, or structural changes in ischemic heart muscle thought to result from reperfusion to the ischemic areas. Changes can be fatal to muscle cells and may include edema with explosive cell swelling and disintegration, sarcolemma disruption, fragmentation of mitochondria, contraction band necrosis, enzyme washout, and calcium overload. Other damage may include hemorrhage and ventricular arrhythmias. One possible mechanism of damage is thought to be oxygen free radicals. Treatment currently includes the introduction of scavengers of oxygen free radicals, and injury is thought to be prevented by warm blood cardioplegic infusion prior to reperfusion. [NIH]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myotonic Dystrophy: A condition presenting muscle weakness and wasting which may be

progressive. [NIH]

Nasal Cavity: The proximal portion of the respiratory passages on either side of the nasal septum, lined with ciliated mucosa, extending from the nares to the pharynx. [NIH]

Nasal Mucosa: The mucous membrane lining the nasal cavity. [NIH]

Nasogastric: The process of passing a small, flexible plastic tube through the nose or mouth into the stomach or small intestine. [NIH]

Nausea: An unpleasant sensation in the stomach usually accompanied by the urge to vomit. Common causes are early pregnancy, sea and motion sickness, emotional stress, intense pain, food poisoning, and various enteroviruses. [NIH]

NCI: National Cancer Institute. NCI, part of the National Institutes of Health of the United States Department of Health and Human Services, is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at http://cancer.gov. [NIH]

Nebulizer: A device used to turn liquid into a fine spray. [NIH]

Necrosis: A pathological process caused by the progressive degradative action of enzymes that is generally associated with severe cellular trauma. It is characterized by mitochondrial swelling, nuclear flocculation, uncontrolled cell lysis, and ultimately cell death. [NIH]

Need: A state of tension or dissatisfaction felt by an individual that impels him to action toward a goal he believes will satisfy the impulse. [NIH]

Neonatal: Pertaining to the first four weeks after birth. [EU]

Neonatal period: The first 4 weeks after birth. [NIH]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

Neoplasm: A new growth of benign or malignant tissue. [NIH]

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Nephrectomy: Surgery to remove a kidney. Radical nephrectomy removes the kidney, the adrenal gland, nearby lymph nodes, and other surrounding tissue. Simple nephrectomy removes only the kidney. Partial nephrectomy removes the tumor but not the entire kidney. [NIH]

Nephropathy: Disease of the kidneys. [EU]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

Nerve Fibers: Slender processes of neurons, especially the prolonged axons that conduct nerve impulses. [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]

Neuroendocrine: Having to do with the interactions between the nervous system and the endocrine system. Describes certain cells that release hormones into the blood in response to stimulation of the nervous system. [NIH]

Neuromuscular: Pertaining to muscles and nerves. [EU]

Neuromuscular Junction: The synapse between a neuron and a muscle. [NIH]

Neuronal: Pertaining to a neuron or neurons (= conducting cells of the nervous system). [EU]

Neurons: The basic cellular units of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system. [NIH]

Neuropeptides: Peptides released by neurons as intercellular messengers. Many neuropeptides are also hormones released by non-neuronal cells. [NIH]

Neurophysiology: The scientific discipline concerned with the physiology of the nervous system. [NIH]

Neuropsychological Tests: Tests designed to assess neurological function associated with certain behaviors. They are used in diagnosing brain dysfunction or damage and central nervous system disorders or injury. [NIH]

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]

Neutrophil: A type of white blood cell. [NIH]

Neutrophil Activation: The process in which the neutrophil is stimulated by diverse substances, resulting in degranulation and/or generation of reactive oxygen products, and culminating in the destruction of invading pathogens. The stimulatory substances, including opsonized particles, immune complexes, and chemotactic factors, bind to specific cell-surface receptors on the neutrophil. [NIH]

Neutrophil Infiltration: The diffusion or accumulation of neutrophils in tissues or cells in response to a wide variety of substances released at the sites of inflammatory reactions. [NIH]

Nicotine: Nicotine is highly toxic alkaloid. It is the prototypical agonist at nicotinic cholinergic receptors where it dramatically stimulates neurons and ultimately blocks synaptic transmission. Nicotine is also important medically because of its presence in tobacco smoke. [NIH]

Nitric Oxide: A free radical gas produced endogenously by a variety of mammalian cells. It is synthesized from arginine by a complex reaction, catalyzed by nitric oxide synthase. Nitric oxide is endothelium-derived relaxing factor. It is released by the vascular endothelium and mediates the relaxation induced by some vasodilators such as acetylcholine and bradykinin. It also inhibits platelet aggregation, induces disaggregation of aggregated platelets, and inhibits platelet adhesion to the vascular endothelium. Nitric oxide activates cytosolic guanylate cyclase and thus elevates intracellular levels of cyclic GMP. [NIH]

Nitrogen: An element with the atomic symbol N, atomic number 7, and atomic weight 14. Nitrogen exists as a diatomic gas and makes up about 78% of the earth's atmosphere by volume. It is a constituent of proteins and nucleic acids and found in all living cells. [NIH]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

Nuclear Medicine: A specialty field of radiology concerned with diagnostic, therapeutic, and investigative use of radioactive compounds in a pharmaceutical form. [NIH]

Nuclear Proteins: Proteins found in the nucleus of a cell. Do not confuse with

nucleoproteins which are proteins conjugated with nucleic acids, that are not necessarily present in the nucleus. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

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]

Nucleoproteins: Proteins conjugated with nucleic acids. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nursing Care: Care given to patients by nursing service personnel. [NIH]

Nutritional Status: State of the body in relation to the consumption and utilization of nutrients. [NIH]

Nutritional Support: The administration of nutrients for assimilation and utilization by a patient by means other than normal eating. It does not include fluid therapy which normalizes body fluids to restore water-electrolyte balance. [NIH]

Observational study: An epidemiologic study that does not involve any intervention, experimental or otherwise. Such a study may be one in which nature is allowed to take its course, with changes in one characteristic being studied in relation to changes in other characteristics. Analytical epidemiologic methods, such as case-control and cohort study designs, are properly called observational epidemiology because the investigator is observing without intervention other than to record, classify, count, and statistically analyze results. [NIH]

Occipital Lobe: Posterior part of the cerebral hemisphere. [NIH]

Occult: Obscure; concealed from observation, difficult to understand. [EU]

Occupational Exposure: The exposure to potentially harmful chemical, physical, or biological agents that occurs as a result of one's occupation. [NIH]

Occupational Health: The promotion and maintenance of physical and mental health in the work environment. [NIH]

Ocular: 1. Of, pertaining to, or affecting the eye. 2. Eyepiece. [EU]

Oculomotor: Cranial nerve III. It originate from the lower ventral surface of the midbrain and is classified as a motor nerve. [NIH]

Oculomotor Nerve: The 3d cranial nerve. The oculomotor nerve sends motor fibers to the levator muscles of the eyelid and to the superior rectus, inferior rectus, and inferior oblique muscles of the eye. It also sends parasympathetic efferents (via the ciliary ganglion) to the muscles controlling pupillary constriction and accommodation. The motor fibers originate in the oculomotor nuclei of the midbrain. [NIH]

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]

Oligo: Chemical and mineral elements that exist in minimal (oligo) quantities in the body, in foods, in the air, in soil; name applied to any element observed as a microconstituent of

plant or animal tissue and of beneficial, harmful, or even doubtful significance. [NIH]

Oligosaccharides: Carbohydrates consisting of between two and ten monosaccharides connected by either an alpha- or beta-glycosidic link. They are found throughout nature in both the free and bound form. [NIH]

Oliguria: Clinical manifestation of the urinary system consisting of a decrease in the amount of urine secreted. [NIH]

Oncogene: A gene that normally directs cell growth. If altered, an oncogene can promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by an environmental exposure to carcinogens. [NIH]

Opacity: Degree of density (area most dense taken for reading). [NIH]

Opsin: A protein formed, together with retinene, by the chemical breakdown of meta-rhodopsin. [NIH]

Optic Chiasm: The X-shaped structure formed by the meeting of the two optic nerves. At the optic chiasm the fibers from the medial part of each retina cross to project to the other side of the brain while the lateral retinal fibers continue on the same side. As a result each half of the brain receives information about the contralateral visual field from both eyes. [NIH]

Optic cup: The white, cup-like area in the center of the optic disc. [NIH]

Optic disc: The circular area (disc) where the optic nerve connects to the retina. [NIH]

Optic Nerve: The 2nd cranial nerve. The optic nerve conveys visual information from the retina to the brain. The nerve carries the axons of the retinal ganglion cells which sort at the optic chiasm and continue via the optic tracts to the brain. The largest projection is to the lateral geniculate nuclei; other important targets include the superior colliculi and the suprachiasmatic nuclei. Though known as the second cranial nerve, it is considered part of the central nervous system. [NIH]

Optic Nerve Diseases: Conditions which produce injury or dysfunction of the second cranial or optic nerve, which is generally considered a component of the central nervous system. Damage to optic nerve fibers may occur at or near their origin in the retina, at the optic disk, or in the nerve, optic chiasm, optic tract, or lateral geniculate nuclei. Clinical manifestations may include decreased visual acuity and contrast sensitivity, impaired color vision, and an afferent pupillary defect. [NIH]

Oral Health: The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [NIH]

Orbit: One of the two cavities in the skull which contains an eyeball. Each eye is located in a bony socket or orbit. [NIH]

Orbital: Pertaining to the orbit (= the bony cavity that contains the eyeball). [EU]

Organ Transplantation: Transference of an organ between individuals of the same species or between individuals of different species. [NIH]

Orofacial: Of or relating to the mouth and face. [EU]

Osteoporosis: Reduction of bone mass without alteration in the composition of bone, leading to fractures. Primary osteoporosis can be of two major types: postmenopausal osteoporosis and age-related (or senile) osteoporosis. [NIH]

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]

Ovalbumin: An albumin obtained from the white of eggs. It is a member of the serpin superfamily. [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]

Overexpress: An excess of a particular protein on the surface of a cell. [NIH]

Ovulation: The discharge of a secondary oocyte from a ruptured graafian follicle. [NIH]

Ovum: A female germ cell extruded from the ovary at ovulation. [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]

Oxygen Consumption: The oxygen consumption is determined by calculating the difference between the amount of oxygen inhaled and exhaled. [NIH]

Oxygenase: Enzyme which breaks down heme, the iron-containing oxygen-carrying constituent of the red blood cells. [NIH]

Oxygenation: The process of supplying, treating, or mixing with oxygen. No:1245 - oxygenation the process of supplying, treating, or mixing with oxygen. [EU]

Pacemaker: An object or substance that influences the rate at which a certain phenomenon occurs; often used alone to indicate the natural cardiac pacemaker or an artificial cardiac pacemaker. In biochemistry, a substance whose rate of reaction sets the pace for a series of interrelated reactions. [EU]

Pachymeningitis: Inflammation of the dura mater of the brain, the spinal cord or the optic nerve. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Pancreatic: Having to do with the pancreas. [NIH]

Pancreatic cancer: Cancer of the pancreas, a salivary gland of the abdomen. [NIH]

Pancreatic Elastase: A protease of broad specificity, obtained from dried pancreas.

Molecular weight is approximately 25,000. The enzyme breaks down elastin, the specific protein of elastic fibers, and digests other proteins such as fibrin, hemoglobin, and albumin. EC 3.4.21.36. [NIH]

Pancreatic Insufficiency: Absence of or reduced pancreatic exocrine secretion into the duodenum and resultant poor digestion of lipids, vitamins, nitrogen, and carbohydrates. [NIH]

Pancreatic Juice: The fluid containing digestive enzymes secreted by the pancreas in response to food in the duodenum. [NIH]

Pancreatitis: Acute or chronic inflammation of the pancreas, which may be asymptomatic or symptomatic, and which is due to autodigestion of a pancreatic tissue by its own enzymes. It is caused most often by alcoholism or biliary tract disease; less commonly it may be associated with hyperlipaemia, hyperparathyroidism, abdominal trauma (accidental or operative injury), vasculitis, or uraemia. [EU]

Panniculitis: General term for inflammation of adipose tissue, usually of the skin, characterized by reddened subcutaneous nodules. [NIH]

Papain: A proteolytic enzyme obtained from Carica papaya. It is also the name used for a purified mixture of papain and chymopapain that is used as a topical enzymatic debriding agent. EC 3.4.22.2. [NIH]

Papilledema: Swelling around the optic disk. [NIH]

Paranasal Sinuses: Air-filled extensions of the respiratory part of the nasal cavity into the frontal, ethmoid, sphenoid, and maxillary cranial bones. They vary in size and form in different individuals and are lined by the ciliated mucous membranes of the nasal cavity. [NIH]

Parasympathetic Nervous System: The craniosacral division of the autonomic nervous system. The cell bodies of the parasympathetic preganglionic fibers are in brain stem nuclei and in the sacral spinal cord. They synapse in cranial autonomic ganglia or in terminal ganglia near target organs. The parasympathetic nervous system generally acts to conserve resources and restore homeostasis, often with effects reciprocal to the sympathetic nervous system. [NIH]

Parenchyma: The essential elements of an organ; used in anatomical nomenclature as a general term to designate the functional elements of an organ, as distinguished from its framework, or stroma. [EU]

Parietal: 1. Of or pertaining to the walls of a cavity. 2. Pertaining to or located near the parietal bone, as the parietal lobe. [EU]

Parotid: The space that contains the parotid gland, the facial nerve, the external carotid artery, and the retromandibular vein. [NIH]

Paroxysmal: Recurring in paroxysms (= spasms or seizures). [EU]

Particle: A tiny mass of material. [EU]

Patch: A piece of material used to cover or protect a wound, an injured part, etc.: a patch over the eye. [NIH]

Pathogenesis: The cellular events and reactions that occur in the development of disease. [NIH]

Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

Pathologies: The study of abnormality, especially the study of diseases. [NIH]

Pathophysiology: Altered functions in an individual or an organ due to disease. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

Patient Selection: Criteria and standards used for the determination of the appropriateness of the inclusion of patients with specific conditions in proposed treatment plans and the criteria used for the inclusion of subjects in various clinical trials and other research protocols. [NIH]

Peak flow: The maximum amount of air breathed out; the power needed to produce this amount. [EU]

Pedigree: A record of one's ancestors, offspring, siblings, and their offspring that may be used to determine the pattern of certain genes or disease inheritance within a family. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Perception: The ability quickly and accurately to recognize similarities and differences among presented objects, whether these be pairs of words, pairs of number series, or multiple sets of these or other symbols such as geometric figures. [NIH]

Percutaneous: Performed through the skin, as injection of radiopacque material in radiological examination, or the removal of tissue for biopsy accomplished by a needle. [EU]

Perforation: 1. The act of boring or piercing through a part. 2. A hole made through a part or substance. [EU]

Perfusion: Bathing an organ or tissue with a fluid. In regional perfusion, a specific area of the body (usually an arm or a leg) receives high doses of anticancer drugs through a blood vessel. Such a procedure is performed to treat cancer that has not spread. [NIH]

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]

Periodicity: The tendency of a phenomenon to recur at regular intervals; in biological systems, the recurrence of certain activities (including hormonal, cellular, neural) may be annual, seasonal, monthly, daily, or more frequently (ultradian). [NIH]

Periodontal disease: Disease involving the supporting structures of the teeth (as the gums and periodontal membranes). [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]

Peripheral Vascular Disease: Disease in the large blood vessels of the arms, legs, and feet. People who have had diabetes for a long time may get this because major blood vessels in their arms, legs, and feet are blocked and these limbs do not receive enough blood. The signs of PVD are aching pains in the arms, legs, and feet (especially when walking) and foot sores that heal slowly. Although people with diabetes cannot always avoid PVD, doctors say they have a better chance of avoiding it if they take good care of their feet, do not smoke, and keep both their blood pressure and diabetes under good control. [NIH]

Peripheral vision: Side vision; ability to see objects and movement outside of the direct line of vision. [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]

Peritoneal Dialysis: Dialysis fluid being introduced into and removed from the peritoneal cavity as either a continuous or an intermittent procedure. [NIH]

Peritoneum: Endothelial lining of the abdominal cavity, the parietal peritoneum covering the inside of the abdominal wall and the visceral peritoneum covering the bowel, the mesentery, and certain of the organs. The portion that covers the bowel becomes the serosal layer of the bowel wall. [NIH]

Peritonitis: Inflammation of the peritoneum; a condition marked by exudations in the peritoneum of serum, fibrin, cells, and pus. It is attended by abdominal pain and tenderness, constipation, vomiting, and moderate fever. [EU]

Petroleum: Naturally occurring complex liquid hydrocarbons which, after distillation, yield combustible fuels, petrochemicals, and lubricants. [NIH]

PH: The symbol relating the hydrogen ion (H+) concentration or activity of a solution to that of a given standard solution. Numerically the pH is approximately equal to the negative logarithm of H+ concentration expressed in molarity. pH 7 is neutral; above it alkalinity increases and below it acidity increases. [EU]

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]

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]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of yeasts. [NIH]

Phenyl: Ingredient used in cold and flu remedies. [NIH]

Phenylalanine: An aromatic amino acid that is essential in the animal diet. It is a precursor of melanin, dopamine, noradrenalin, and thyroxine. [NIH]

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]

Phospholipids: Lipids containing one or more phosphate groups, particularly those derived from either glycerol (phosphoglycerides; glycerophospholipids) or sphingosine (sphingolipids). They are polar lipids that are of great importance for the structure and function of cell membranes and are the most abundant of membrane lipids, although not stored in large amounts in the system. [NIH]

Phosphorus: A non-metallic element that is found in the blood, muscles, nevers, bones, and

teeth, and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells.) [NIH]

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]

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]

Photoreceptor: Receptor capable of being activated by light stimuli, as a rod or cone cell of the eye. [NIH]

Phototherapy: Treatment of disease by exposure to light, especially by variously concentrated light rays or specific wavelengths. [NIH]

Phototransduction: The transducing of light energy to afferent nerve impulses, such as takes place in the retinal rods and cones. After light photons are absorbed by the photopigments, the signal is transmitted to the outer segment membrane by the cyclic GMP second messenger system, where it closes the sodium channels. This channel gating ultimately generates an action potential in the inner retina. [NIH]

Physical Medicine: A medical specialty concerned with the use of physical agents, mechanical apparatus, and manipulation in rehabilitating physically diseased or injured patients. [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 study: The initial study examining a new method or treatment. [NIH]

Pitch: The subjective awareness of the frequency or spectral distribution of a sound. [NIH]

Plants: Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

Plaque: A clear zone in a bacterial culture grown on an agar plate caused by localized destruction of bacterial cells by a bacteriophage. The concentration of infective virus in a fluid can be estimated by applying the fluid to a culture and counting the number of. [NIH]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

Plasma protein: One of the hundreds of different proteins present in blood plasma, including carrier proteins (such albumin, transferrin, and haptoglobin), fibrinogen and other coagulation factors, complement components, immunoglobulins, enzyme inhibitors, precursors of substances such as angiotension and bradykinin, and many other types of proteins. [EU]

Plasma Volume: Volume of plasma in the circulation. It is usually measured by indicator

dilution techniques. [NIH]

Plasmid: An autonomously replicating, extra-chromosomal DNA molecule found in many bacteria. Plasmids are widely used as carriers of cloned genes. [NIH]

Plasmin: A product of the lysis of plasminogen (profibrinolysin) by plasminogen activators. It is composed of two polypeptide chains, light (B) and heavy (A), with a molecular weight of 75,000. It is the major proteolytic enzyme involved in blood clot retraction or the lysis of fibrin and quickly inactivated by antiplasmins. EC 3.4.21.7. [NIH]

Plasminogen: Precursor of fibrinolysin (plasmin). It is a single-chain beta-globulin of molecular weight 80-90,000 found mostly in association with fibrinogen in plasma; plasminogen activators change it to fibrinolysin. It is used in wound debriding and has been investigated as a thrombolytic agent. [NIH]

Plasminogen Activators: A heterogeneous group of proteolytic enzymes that convert plasminogen to plasmin. They are concentrated in the lysosomes of most cells and in the vascular endothelium, particularly in the vessels of the microcirculation. EC 3.4.21.-. [NIH]

Plasminogen Inactivators: Important modulators of the activity of plasminogen activators. Four inhibitors, all belonging to the serpin family of proteins, have been implicated in plasminogen activation inhibition. They are PAI-1, PAI-2, protease-nexin, and protein C inhibitor (PAI-3). All inhibit both the tissue-type and urokinase-type plasminogen activators. [NIH]

Platelet Activation: A series of progressive, overlapping events triggered by exposure of the platelets to subendothelial tissue. These events include shape change, adhesiveness, aggregation, and release reactions. When carried through to completion, these events lead to the formation of a stable hemostatic plug. [NIH]

Platelet Aggregation: The attachment of platelets to one another. This clumping together can be induced by a number of agents (e.g., thrombin, collagen) and is part of the mechanism leading to the formation of a thrombus. [NIH]

Platelet Factor 4: A high-molecular-weight proteoglycan-platelet factor complex which is released from blood platelets by thrombin. It acts as a mediator in the heparin-neutralizing capacity of the blood and plays a role in platelet aggregation. At high ionic strength (I=0.75), the complex dissociates into the active component (molecular weight 29,000) and the proteoglycan carrier (chondroitin 4-sulfate, molecular weight 350,000). The molecule exists in the form of a dimer consisting of 8 moles of platelet factor 4 and 2 moles of proteoglycan. [NIH]

Platelets: A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called thrombocytes. [NIH]

Platinum: Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

Plethysmography: Recording of change in the size of a part as modified by the circulation in it. [NIH]

Pleura: The thin serous membrane enveloping the lungs and lining the thoracic cavity. [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]

Pneumology: The study of disease of the air passages. [NIH]

Pneumonectomy: An operation to remove an entire lung. [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]

Point Mutation: A mutation caused by the substitution of one nucleotide for another. This results in the DNA molecule having a change in a single base pair. [NIH]

Pollen: The male fertilizing element of flowering plants analogous to sperm in animals. It is released from the anthers as yellow dust, to be carried by insect or other vectors, including wind, to the ovary (stigma) of other flowers to produce the embryo enclosed by the seed. The pollens of many plants are allergenic. [NIH]

Polycystic: An inherited disorder characterized by many grape-like clusters of fluid-filled cysts that make both kidneys larger over time. These cysts take over and destroy working kidney tissue. PKD may cause chronic renal failure and end-stage renal disease. [NIH]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand as a template. The polymerase copies the template in the 5'-3'direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

Polymerase Chain Reaction: In vitro method for producing large amounts of specific DNA or RNA fragments of defined length and sequence from small amounts of short oligonucleotide flanking sequences (primers). The essential steps include thermal denaturation of the double-stranded target molecules, annealing of the primers to their complementary sequences, and extension of the annealed primers by enzymatic synthesis with DNA polymerase. The reaction is efficient, specific, and extremely sensitive. Uses for the reaction include disease diagnosis, detection of difficult-to-isolate pathogens, mutation analysis, genetic testing, DNA sequencing, and analyzing evolutionary relationships. [NIH]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

Polyp: A growth that protrudes from a mucous membrane. [NIH]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

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]

Postmenopausal: Refers to the time after menopause. Menopause is the time in a woman's life when menstrual periods stop permanently; also called "change of life." [NIH]

Postnatal: Occurring after birth, with reference to the newborn. [EU]

Postoperative: After surgery. [NIH]

Postsynaptic: Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

Potentiation: An overall effect of two drugs taken together which is greater than the sum of the effects of each drug taken alone. [NIH]

Practicability: A non-standard characteristic of an analytical procedure. It is dependent on the scope of the method and is determined by requirements such as sample throughout and costs. [NIH]

Practice Guidelines: Directions or principles presenting current or future rules of policy for the health care practitioner to assist him in patient care decisions regarding diagnosis, therapy, or related clinical circumstances. The guidelines may be developed by government agencies at any level, institutions, professional societies, governing boards, or by the convening of expert panels. The guidelines form a basis for the evaluation of all aspects of health care and delivery. [NIH]

Precancerous: A term used to describe a condition that may (or is likely to) become cancer. Also called premalignant. [NIH]

Precipitating Factors: Factors associated with the definitive onset of a disease, illness, accident, behavioral response, or course of action. Usually one factor is more important or more obviously recognizable than others, if several are involved, and one may often be regarded as "necessary". Examples include exposure to specific disease; amount or level of an infectious organism, drug, or noxious agent, etc. [NIH]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Predisposition: A latent susceptibility to disease which may be activated under certain conditions, as by stress. [EU]

Premalignant: A term used to describe a condition that may (or is likely to) become cancer. Also called precancerous. [NIH]

Presynaptic: Situated proximal to a synapse, or occurring before the synapse is crossed. [EU]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Prion: Small proteinaceous infectious particles that resist inactivation by procedures modifying nucleic acids and contain an abnormal isoform of a cellular protein which is a major and necessary component. [NIH]

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]

Prodrug: A substance that gives rise to a pharmacologically active metabolite, although not itself active (i. e. an inactive precursor). [NIH]

Proenzyme: 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]

Progeny: The offspring produced in any generation. [NIH]

Progression: Increase in the size of a tumor or spread of cancer in the body. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

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]

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]

Prostate: A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

Protease Inhibitors: Compounds which inhibit or antagonize biosynthesis or actions of proteases (endopeptidases). [NIH]

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 Folding: A rapid biochemical reaction involved in the formation of proteins. It begins even before a protein has been completely synthesized and proceeds through discrete intermediates (primary, secondary, and tertiary structures) before the final structure (quaternary structure) is developed. [NIH]

Protein S: The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

Proteoglycan: A molecule that contains both protein and glycosaminoglycans, which are a type of polysaccharide. Proteoglycans are found in cartilage and other connective tissues. [NIH]

Proteolytic: 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Prothrombin: A plasma protein that is the inactive precursor of thrombin. It is converted to thrombin by a prothrombin activator complex consisting of factor Xa, factor V, phospholipid, and calcium ions. Deficiency of prothrombin leads to hypoprothrombinemia. [NIH]

Protocol: The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other

aspects of trial design. [NIH]

Protons: Stable elementary particles having the smallest known positive charge, found in the nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

Protozoa: A subkingdom consisting of unicellular organisms that are the simplest in the animal kingdom. Most are free living. They range in size from submicroscopic to macroscopic. Protozoa are divided into seven phyla: Sarcomastigophora, Labyrinthomorpha, Apicomplexa, Microspora, Ascetospora, Myxozoa, and Ciliophora. [NIH]

Proximal: Nearest; closer to any point of reference; opposed to distal. [EU]

Pseudomonas: A genus of gram-negative, aerobic, rod-shaped bacteria widely distributed in nature. Some species are pathogenic for humans, animals, and plants. [NIH]

Pseudotumor Cerebri: A condition marked by raised intracranial pressure and characterized clinically by headaches; nausea; papilledema, peripheral constriction of the visual fields, transient visual obscurations, and pulsatile tinnitus. Obesity is frequently associated with this condition, which primarily affects women between 20 and 44 years of age. Chronic papilledema may lead to optic nerve injury (optic nerve diseases) and visual loss (blindness). [NIH]

Psoriasis: A common genetically determined, chronic, inflammatory skin disease characterized by rounded erythematous, dry, scaling patches. The lesions have a predilection for nails, scalp, genitalia, extensor surfaces, and the lumbosacral region. Accelerated epidermopoiesis is considered to be the fundamental pathologic feature in psoriasis. [NIH]

Psychiatry: The medical science that deals with the origin, diagnosis, prevention, and treatment of mental disorders. [NIH]

Public Health: Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the international, national, state, or municipal level. [NIH]

Public Policy: A course or method of action selected, usually by a government, from among alternatives to guide and determine present and future decisions. [NIH]

Publishing: "The business or profession of the commercial production and issuance of literature" (Webster's 3d). It includes the publisher, publication processes, editing and editors. Production may be by conventional printing methods or by electronic publishing. [NIH]

Pulmonary: Relating to the lungs. [NIH]

Pulmonary Artery: The short wide vessel arising from the conus arteriosus of the right ventricle and conveying unaerated blood to the lungs. [NIH]

Pulmonary Circulation: The circulation of blood through the lungs. [NIH]

Pulmonary Edema: An accumulation of an excessive amount of watery fluid in the lungs, may be caused by acute exposure to dangerous concentrations of irritant gasses. [NIH]

Pulmonary Embolism: Embolism in the pulmonary artery or one of its branches. [NIH]

Pulmonary Emphysema: Condition of the lungs characterized by increase beyond normal in the size of air spaces distal to the terminal bronchioles, either from dilatation of the alveoli or from destruction of their walls. [NIH]

Pulmonary Fibrosis: Chronic inflammation and progressive fibrosis of the pulmonary alveolar walls, with steadily progressive dyspnea, resulting finally in death from oxygen lack or right heart failure. [NIH]

Pulmonary hypertension: Abnormally high blood pressure in the arteries of the lungs. [NIH]

Pulmonary Ventilation: The total volume of gas per minute inspired or expired measured in liters per minute. [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]

Pyelitis: Inflammation of the pelvis of the kidney. It is attended by pain and tenderness in the loins, irritability of the bladder, remittent fever, bloody or purulent urine, diarrhoea, vomiting, and a peculiar pain on flexion of the thigh. [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]

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]

Quaternary: 1. Fourth in order. 2. Containing four elements or groups. [EU]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

Radiation therapy: The use of high-energy radiation from x-rays, gamma rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body in the area near cancer cells (internal radiation therapy, implant radiation, or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy. [NIH]

Radioactive: Giving off radiation. [NIH]

Radiography: Examination of any part of the body for diagnostic purposes by means of roentgen rays, recording the image on a sensitized surface (such as photographic film). [NIH]

Radiolabeled: Any compound that has been joined with a radioactive substance. [NIH]

Radiological: Pertaining to radiodiagnostic and radiotherapeutic procedures, and interventional radiology or other planning and guiding medical radiology. [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]

Radiotherapy: The use of ionizing radiation to treat malignant neoplasms and other benign conditions. The most common forms of ionizing radiation used as therapy are x-rays, gamma rays, and electrons. A special form of radiotherapy, targeted radiotherapy, links a

cytotoxic radionuclide to a molecule that targets the tumor. When this molecule is an antibody or other immunologic molecule, the technique is called radioimmunotherapy. [NIH]

Random Allocation: A process involving chance used in therapeutic trials or other research endeavor for allocating experimental subjects, human or animal, between treatment and control groups, or among treatment groups. It may also apply to experiments on inanimate objects. [NIH]

Randomization: Also called random allocation. Is allocation of individuals to groups, e.g., for experimental and control regimens, by chance. Within the limits of chance variation, random allocation should make the control and experimental groups similar at the start of an investigation and ensure that personal judgment and prejudices of the investigator do not influence allocation. [NIH]

Randomized: Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

Reactive Oxygen Species: Reactive intermediate oxygen species including both radicals and non-radicals. These substances are constantly formed in the human body and have been shown to kill bacteria and inactivate proteins, and have been implicated in a number of diseases. Scientific data exist that link the reactive oxygen species produced by inflammatory phagocytes to cancer development. [NIH]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Receptor: A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

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]

Rectum: The last 8 to 10 inches of the large intestine. [NIH]

Recur: To occur again. Recurrence is the return of cancer, at the same site as the original (primary) tumor or in another location, after the tumor had disappeared. [NIH]

Recurrence: The return of a sign, symptom, or disease after a remission. [NIH]

Red blood cells: RBCs. Cells that carry oxygen to all parts of the body. Also called erythrocytes. [NIH]

Red Nucleus: A pinkish-yellow portion of the midbrain situated in the rostral mesencephalic tegmentum. It receives a large projection from the contralateral half of the cerebellum via the superior cerebellar peduncle and a projection from the ipsilateral motor cortex. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

Reflex: An involuntary movement or exercise of function in a part, excited in response to a stimulus applied to the periphery and transmitted to the brain or spinal cord. [NIH]

Reflux: The term used when liquid backs up into the esophagus from the stomach. [NIH]

Refraction: A test to determine the best eyeglasses or contact lenses to correct a refractive error (myopia, hyperopia, or astigmatism). [NIH]

Refractive Errors: Deviations from the average or standard indices of refraction of the eye through its dioptric or refractive apparatus. [NIH]

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]

Rehabilitative: Instruction of incapacitated individuals or of those affected with some mental disorder, so that some or all of their lost ability may be regained. [NIH]

Renal failure: Progressive renal insufficiency and uremia, due to irreversible and progressive renal glomerular tubular or interstitial disease. [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]

Reperfusion: Restoration of blood supply to tissue which is ischemic due to decrease in normal blood supply. The decrease may result from any source including atherosclerotic obstruction, narrowing of the artery, or surgical clamping. It is primarily a procedure for treating infarction or other ischemia, by enabling viable ischemic tissue to recover, thus limiting further necrosis. However, it is thought that reperfusion can itself further damage the ischemic tissue, causing reperfusion injury. [NIH]

Reperfusion Injury: Functional, metabolic, or structural changes, including necrosis, in ischemic tissues thought to result from reperfusion to ischemic areas of the tissue. The most common instance is myocardial reperfusion injury. [NIH]

Resected: Surgical removal of part of an organ. [NIH]

Resection: Removal of tissue or part or all of an organ by surgery. [NIH]

Residential Facilities: Long-term care facilities which provide supervision and assistance in activities of daily living with medical and nursing services when required. [NIH]

Resolving: The ability of the eye or of a lens to make small objects that are close together, separately visible; thus revealing the structure of an object. [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]

Respirable: Dust particles smaller than 0. 005 mm, which are deposited in the respiratory region of the lungs. [NIH]

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 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]

Respiratory Mechanics: The physical or mechanical action of the lungs, diaphragm, ribs, and chest wall during respiration. It includes airflow, lung volume, neural and reflex controls, mechanoreceptors, breathing patterns, etc. [NIH]

Respiratory Muscles: These include the muscles of the diaphragm and the intercostal muscles. [NIH]

Respiratory Physiology: Functions and activities of the respiratory tract as a whole or of any of its parts. [NIH]

Respiratory syncytial virus: RSV. A virus that causes respiratory infections with cold-like symptoms. [NIH]

Respiratory System: The tubular and cavernous organs and structures, by means of which pulmonary ventilation and gas exchange between ambient air and the blood are brought about. [NIH]

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]

Retina: The ten-layered nervous tissue membrane of the eye. It is continuous with the optic nerve and receives images of external objects and transmits visual impulses to the brain. Its outer surface is in contact with the choroid and the inner surface with the vitreous body. The outer-most layer is pigmented, whereas the inner nine layers are transparent. [NIH]

Retinal: 1. Pertaining to the retina. 2. The aldehyde of retinol, derived by the oxidative enzymatic splitting of absorbed dietary carotene, and having vitamin A activity. In the retina, retinal combines with opsins to form visual pigments. One isomer, 11-cis retinal combines with opsin in the rods (scotopsin) to form rhodopsin, or visual purple. Another, all-trans retinal (trans-r.); visual yellow; xanthopsin) results from the bleaching of rhodopsin by light, in which the 11-cis form is converted to the all-trans form. Retinal also combines with opsins in the cones (photopsins) to form the three pigments responsible for colour vision. Called also retinal, and retinene1. [EU]

Retinal Ganglion Cells: Cells of the innermost nuclear layer of the retina, the ganglion cell layer, which project axons through the optic nerve to the brain. They are quite variable in size and in the shapes of their dendritic arbors, which are generally confined to the inner plexiform layer. [NIH]

Retinoblastoma: An eye cancer that most often occurs in children younger than 5 years. It occurs in hereditary and nonhereditary (sporadic) forms. [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]

Retroperitoneal: Having to do with the area outside or behind the peritoneum (the tissue that lines the abdominal wall and covers most of the organs in the abdomen). [NIH]

Retrospective: Looking back at events that have already taken place. [NIH]

Retroviral vector: RNA from a virus that is used to insert genetic material into cells. [NIH]

Reverberant: The sound field prevailing in a large enclosure with moderately reflecting surfaces. [NIH]

Rheumatism: A group of disorders marked by inflammation or pain in the connective tissue

structures of the body. These structures include bone, cartilage, and fat. [NIH]

Rheumatoid: Resembling rheumatism. [EU]

Rheumatoid arthritis: A form of arthritis, the cause of which is unknown, although infection, hypersensitivity, hormone imbalance and psychologic stress have been suggested as possible causes. [NIH]

Rhinitis: Inflammation of the mucous membrane of the nose. [NIH]

Ribonuclease: RNA-digesting enzyme. [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]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Rod: A reception for vision, located in the retina. [NIH]

Root Canal Therapy: A treatment modality in endodontics concerned with the therapy of diseases of the dental pulp. For preparatory procedures, root canal preparation is available. [NIH]

Rural Population: The inhabitants of rural areas or of small towns classified as rural. [NIH]

Saline: A solution of salt and water. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Sarcoid: A cutaneus lesion occurring as a manifestation of sarcoidosis. [NIH]

Sarcoidosis: An idiopathic systemic inflammatory granulomatous disorder comprised of epithelioid and multinucleated giant cells with little necrosis. It usually invades the lungs with fibrosis and may also involve lymph nodes, skin, liver, spleen, eyes, phalangeal bones, and parotid glands. [NIH]

Saturate: Means fatty acids without double bond. [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]

Scleroderma: A chronic disorder marked by hardening and thickening of the skin.

Scleroderma can be localized or it can affect the entire body (systemic). [NIH]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Scoliosis: A lateral curvature of the spine. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Scrotum: In males, the external sac that contains the testicles. [NIH]

Sebaceous: Gland that secretes sebum. [NIH]

Sebaceous gland: Gland that secretes sebum. [NIH]

Secondary tumor: Cancer that has spread from the organ in which it first appeared to another organ. For example, breast cancer cells may spread (metastasize) to the lungs and cause the growth of a new tumor. When this happens, the disease is called metastatic breast cancer, and the tumor in the lungs is called a secondary tumor. Also called secondary cancer. [NIH]

Secretion: 1. The process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. Any substance produced by secretion. [EU]

Secretory: Secreting; relating to or influencing secretion or the secretions. [NIH]

Segmentation: The process by which muscles in the intestines move food and wastes through the body. [NIH]

Segregation: The separation in meiotic cell division of homologous chromosome pairs and their contained allelomorphic gene pairs. [NIH]

Seizures: Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena. Recurrent seizures are usually referred to as epilepsy or "seizure disorder." [NIH]

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]

Senile: Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

Sensitization: 1. Administration of antigen to induce a primary immune response; priming; immunization. 2. Exposure to allergen that results in the development of hypersensitivity. 3. The coating of erythrocytes with antibody so that they are subject to lysis by complement in the presence of homologous antigen, the first stage of a complement fixation test. [EU]

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]

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]

Serine Endopeptidases: Any member of the group of endopeptidases containing at the active site a serine residue involved in catalysis. EC 3.4.21. [NIH]

Serine Proteinase Inhibitors: Exogenous or endogenous compounds which inhibit serine endopeptidases. [NIH]

Serous: Having to do with serum, the clear liquid part of blood. [NIH]

Serpins: A family of serine proteinase inhibitors which are similar in amino acid sequence and mechanism of inhibition, but differ in their specificity toward proteolytic enzymes. This family includes alpha 1-antitrypsin, angiotensinogen, ovalbumin, antiplasmin, alpha 1-antichymotrypsin, thyroxine-binding protein, complement 1 inactivators, antithrombin III, heparin cofactor II, plasminogen inactivators, gene Y protein, placental plasminogen activator inhibitor, and barley Z protein. Some members of the serpin family may be substrates rather than inhibitors of serine endopeptidases, and some serpins occur in plants where their function is not known. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Sex Determination: The biological characteristics which distinguish human beings as female or male. [NIH]

Shock: The general bodily disturbance following a severe injury; an emotional or moral upset occasioned by some disturbing or unexpected experience; disruption of the circulation, which can upset all body functions: sometimes referred to as circulatory shock. [NIH]

Side effect: A consequence other than the one(s) for which an agent or measure is used, as the adverse effects produced by a drug, especially on a tissue or organ system other than the one sought to be benefited by its administration. [EU]

Sigmoid: 1. Shaped like the letter S or the letter C. 2. The sigmoid colon. [EU]

Sigmoid Colon: The lower part of the colon that empties into the rectum. [NIH]

Sigmoidoscopy: Endoscopic examination, therapy or surgery of the sigmoid flexure. [NIH]

Signal Transduction: The intercellular or intracellular transfer of information (biological activation/inhibition) through a signal pathway. In each signal transduction system, an activation/inhibition signal from a biologically active molecule (hormone, neurotransmitter) is mediated via the coupling of a receptor/enzyme to a second messenger system or to an ion channel. Signal transduction plays an important role in activating cellular functions, cell differentiation, and cell proliferation. Examples of signal transduction systems are the GABA-postsynaptic receptor-calcium ion channel system, the receptor-mediated T-cell activation pathway, and the receptor-mediated activation of phospholipases. Those coupled to membrane depolarization or intracellular release of calcium include the receptor-mediated activation of cytotoxic functions in granulocytes and the synaptic potentiation of protein kinase activation. Some signal transduction pathways may be part of larger signal transduction pathways; for example, protein kinase activation is part of the platelet activation signal pathway. [NIH]

Signs and Symptoms: Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [NIH]

Sinusitis: An inflammatory process of the mucous membranes of the paranasal sinuses that occurs in three stages: acute, subacute, and chronic. Sinusitis results from any condition

causing ostial obstruction or from pathophysiologic changes in the mucociliary transport mechanism. [NIH]

Skeletal: Having to do with the skeleton (boney part of the body). [NIH]

Skeleton: The framework that supports the soft tissues of vertebrate animals and protects many of their internal organs. The skeletons of vertebrates are made of bone and/or cartilage. [NIH]

Skull: The skeleton of the head including the bones of the face and the bones enclosing the brain. [NIH]

Sleep apnea: A serious, potentially life-threatening breathing disorder characterized by repeated cessation of breathing due to either collapse of the upper airway during sleep or absence of respiratory effort. [NIH]

Small intestine: The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

Smooth muscle: Muscle that performs automatic tasks, such as constricting blood vessels. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

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]

Solitary Nucleus: Gray matter located in the dorsomedial part of the medulla oblongata associated with the solitary tract. The solitary nucleus receives inputs from most organ systems including the terminations of the facial, glossopharyngeal, and vagus nerves. It is a major coordinator of autonomic nervous system regulation of cardiovascular, respiratory, gustatory, gastrointestinal, and chemoreceptive aspects of homeostasis. The solitary nucleus is also notable for the large number of neurotransmitters which are found therein. [NIH]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Specialist: In medicine, one who concentrates on 1 special branch of medical science. [NIH]

Species: A taxonomic category subordinate to a genus (or subgenus) and superior to a subspecies or variety, composed of individuals possessing common characters distinguishing them from other categories of individuals of the same taxonomic level. In taxonomic nomenclature, species are designated by the genus name followed by a Latin or Latinized adjective or noun. [EU]

Specificity: Degree of selectivity shown by an antibody with respect to the number and types of antigens with which the antibody combines, as well as with respect to the rates and the extents of these reactions. [NIH]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of

a disease. [EU]

Sperm: The fecundating fluid of the male. [NIH]

Sphenoid: An unpaired cranial bone with a body containing the sphenoid sinus and forming the posterior part of the medial walls of the orbits. [NIH]

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]

Spirometry: Measurement of volume of air inhaled or exhaled by the lung. [NIH]

Spleen: An organ that is part of the lymphatic system. The spleen produces lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach. [NIH]

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]

Sputum: The material expelled from the respiratory passages by coughing or clearing the throat. [NIH]

Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

Steel: A tough, malleable, iron-based alloy containing up to, but no more than, two percent carbon and often other metals. It is used in medicine and dentistry in implants and instrumentation. [NIH]

Stem cell transplantation: A method of replacing immature blood-forming cells that were destroyed by cancer treatment. The stem cells are given to the person after treatment to help the bone marrow recover and continue producing healthy blood cells. [NIH]

Stem Cells: Relatively undifferentiated cells of the same lineage (family type) that retain the ability to divide and cycle throughout postnatal life to provide cells that can become specialized and take the place of those that die or are lost. [NIH]

Steroids: Drugs used to relieve swelling and inflammation. [NIH]

Stimulus: That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Strabismus: Deviation of the eye which the patient cannot overcome. The visual axes assume a position relative to each other different from that required by the physiological conditions. The various forms of strabismus are spoken of as tropias, their direction being indicated by the appropriate prefix, as cyclo tropia, esotropia, exotropia, hypertropia, and hypotropia. Called also cast, heterotropia, manifest deviation, and squint. [EU]

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]

Streptokinase: Streptococcal fibrinolysin . An enzyme produced by hemolytic streptococci. It hydrolyzes amide linkages and serves as an activator of plasminogen. It is used in thrombolytic therapy and is used also in mixtures with streptodornase (streptodornase and streptokinase). EC 3.4.-. [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]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Stroma: The middle, thickest layer of tissue in the cornea. [NIH]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subcapsular: Situated below a capsule. [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]

Subcutaneous Emphysema: Presence of air or gas in the subcutaneous tissues of the body. [NIH]

Submaxillary: Four to six lymph glands, located between the lower jaw and the submandibular salivary gland. [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]

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]

Superoxide: Derivative of molecular oxygen that can damage cells. [NIH]

Superoxide Dismutase: An oxidoreductase that catalyzes the reaction between superoxide anions and hydrogen to yield molecular oxygen and hydrogen peroxide. The enzyme protects the cell against dangerous levels of superoxide. EC 1.15.1.1. [NIH]

Supplementation: Adding nutrients to the diet. [NIH]

Surfactant: A fat-containing protein in the respiratory passages which reduces the surface tension of pulmonary fluids and contributes to the elastic properties of pulmonary tissue. [NIH]

Survival Rate: The proportion of survivors in a group, e.g., of patients, studied and followed over a period, or the proportion of persons in a specified group alive at the

beginning of a time interval who survive to the end of the interval. It is often studied using life table methods. [NIH]

Suspensions: Colloids with liquid continuous phase and solid dispersed phase; the term is used loosely also for solid-in-gas (aerosol) and other colloidal systems; water-insoluble drugs may be given as suspensions. [NIH]

Sweat: The fluid excreted by the sweat glands. It consists of water containing sodium chloride, phosphate, urea, ammonia, and other waste products. [NIH]

Sweat Glands: Sweat-producing structures that are embedded in the dermis. Each gland consists of a single tube, a coiled body, and a superficial duct. [NIH]

Sympathetic Nervous System: The thoracolumbar division of the autonomic nervous system. Sympathetic preganglionic fibers originate in neurons of the intermediolateral column of the spinal cord and project to the paravertebral and prevertebral ganglia, which in turn project to target organs. The sympathetic nervous system mediates the body's response to stressful situations, i.e., the fight or flight reactions. It often acts reciprocally to the parasympathetic system. [NIH]

Symphysis: A secondary cartilaginous joint. [NIH]

Symptomatic: Having to do with symptoms, which are signs of a condition or disease. [NIH]

Synapsis: The pairing between homologous chromosomes of maternal and paternal origin during the prophase of meiosis, leading to the formation of gametes. [NIH]

Synaptic: Pertaining to or affecting a synapse (= site of functional apposition between neurons, at which an impulse is transmitted from one neuron to another by electrical or chemical means); pertaining to synapsis (= pairing off in point-for-point association of homologous chromosomes from the male and female pronuclei during the early prophase of meiosis). [EU]

Synaptic Transmission: The communication from a neuron to a target (neuron, muscle, or secretory cell) across a synapse. In chemical synaptic transmission, the presynaptic neuron releases a neurotransmitter that diffuses across the synaptic cleft and binds to specific synaptic receptors. These activated receptors modulate ion channels and/or second-messenger systems to influence the postsynaptic cell. Electrical transmission is less common in the nervous system, and, as in other tissues, is mediated by gap junctions. [NIH]

Synaptophysin: A 38-kDa integral membrane glycoprotein of the presynaptic vesicles in neuron and neuroendocrine cells. It is expressed by a variety of normal and neoplastic neuroendocrine cells and is therefore used as an immunocytochemical marker for neuroendocrine differentiation in various tumors. In Alzheimer disease and other dementing disorders there is an important synapse loss due in part to a decrease of synaptophysin in the presynaptic vesicles. [NIH]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Systemic: Affecting the entire body. [NIH]

Systolic: Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

Tachypnea: Rapid breathing. [NIH]

Tear Gases: Gases that irritate the eyes, throat, or skin. Severe lacrimation develops upon irritation of the eyes. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

Temporal: One of the two irregular bones forming part of the lateral surfaces and base of the

skull, and containing the organs of hearing. [NIH]

Teratogenic: Tending to produce anomalies of formation, or teratism (= anomaly of formation or development : condition of a monster). [EU]

Testicles: The two egg-shaped glands found inside the scrotum. They produce sperm and male hormones. Also called testes. [NIH]

Thalamic: Cell that reaches the lateral nucleus of amygdala. [NIH]

Thalamic Diseases: Disorders of the centrally located thalamus, which integrates a wide range of cortical and subcortical information. Manifestations include sensory loss, movement disorders; ataxia, pain syndromes, visual disorders, a variety of neuropsychological conditions, and coma. Relatively common etiologies include cerebrovascular disorders; craniocerebral trauma; brain neoplasms; brain hypoxia; intracranial hemorrhages; and infectious processes. [NIH]

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]

Thigh: A leg; in anatomy, any elongated process or part of a structure more or less comparable to a leg. [NIH]

Thoracic: Having to do with the chest. [NIH]

Thoracic Surgery: A surgical specialty concerned with diagnosis and treatment of disorders of the heart, lungs, and esophagus. Two major types of thoracic surgery are classified as pulmonary and cardiovascular. [NIH]

Thoracotomy: Surgical incision into the chest wall. [NIH]

Thorax: A part of the trunk between the neck and the abdomen; the chest. [NIH]

Threonine: An essential amino acid occurring naturally in the L-form, which is the active form. It is found in eggs, milk, gelatin, and other proteins. [NIH]

Threshold: For a specified sensory modality (e. g. light, sound, vibration), the lowest level (absolute threshold) or smallest difference (difference threshold, difference limen) or intensity of the stimulus discernible in prescribed conditions of stimulation. [NIH]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombolytic: 1. Dissolving or splitting up a thrombus. 2. A thrombolytic agent. [EU]

Thrombolytic Therapy: Use of infusions of fibrinolytic agents to destroy or dissolve thrombi in blood vessels or bypass grafts. [NIH]

Thrombomodulin: A cell surface glycoprotein of endothelial cells that binds thrombin and serves as a cofactor in the activation of protein C and its regulation of blood coagulation. [NIH]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thrombus: An aggregation of blood factors, primarily platelets and fibrin with entrapment of cellular elements, frequently causing vascular obstruction at the point of its formation. Some authorities thus differentiate thrombus formation from simple coagulation or clot formation. [EU]

Thymidine: A chemical compound found in DNA. Also used as treatment for mucositis. [NIH]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [NIH]

Thyroxine: An amino acid of the thyroid gland which exerts a stimulating effect on thyroid metabolism. [NIH]

Tinnitus: Sounds that are perceived in the absence of any external noise source which may take the form of buzzing, ringing, clicking, pulsations, and other noises. Objective tinnitus refers to noises generated from within the ear or adjacent structures that can be heard by other individuals. The term subjective tinnitus is used when the sound is audible only to the affected individual. Tinnitus may occur as a manifestation of cochlear diseases; vestibulocochlear nerve diseases; intracranial hypertension; craniocerebral trauma; and other conditions. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Tolerance: 1. The ability to endure unusually large doses of a drug or toxin. 2. Acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

Tomography: Imaging methods that result in sharp images of objects located on a chosen plane and blurred images located above or below the plane. [NIH]

Tonometer: For testing the intra-ocular tension. [NIH]

Tonometry: The standard to determine the fluid pressure inside the eye (intraocular pressure). [NIH]

Tooth Preparation: Procedures carried out with regard to the teeth or tooth structures preparatory to specified dental therapeutic and surgical measures. [NIH]

Topical: On the surface of the body. [NIH]

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]

Trachea: The cartilaginous and membranous tube descending from the larynx and branching into the right and left main bronchi. [NIH]

Tracheostomy: Surgical formation of an opening into the trachea through the neck, or the opening so created. [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]

Transgenes: Genes that are introduced into an organism using gene transfer techniques. [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]

Translocate: The attachment of a fragment of one chromosome to a non-homologous chromosome. [NIH]

Transmitter: A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [NIH]

Transplantation: Transference of a tissue or organ, alive or dead, within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Trauma: Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [NIH]

Tremor: Cyclical movement of a body part that can represent either a physiologic process or a manifestation of disease. Intention or action tremor, a common manifestation of cerebellar diseases, is aggravated by movement. In contrast, resting tremor is maximal when there is no attempt at voluntary movement, and occurs as a relatively frequent manifestation of Parkinson disease. [NIH]

Triad: Trivalent. [NIH]

Triglyceride: A lipid carried through the blood stream to tissues. Most of the body's fat tissue is in the form of triglycerides, stored for use as energy. Triglycerides are obtained primarily from fat in foods. [NIH]

Trochlear Nerve: The 4th cranial nerve. The trochlear nerve carries the motor innervation of the superior oblique muscles of the eye. [NIH]

Trochlear Nerve Diseases: Diseases of the fourth cranial (trochlear) nerve or its nucleus in the midbrain. The nerve crosses as it exits the midbrain dorsally and may be injured along its course through the intracranial space, cavernous sinus, superior orbital fissure, or orbit. Clinical manifestations include weakness of the superior oblique muscle which causes vertical diplopia that is maximal when the affected eye is adducted and directed inferiorly. Head tilt may be seen as a compensatory mechanism for diplopia and rotation of the visual axis. Common etiologies include craniocerebral trauma and infratentorial neoplasms. [NIH]

Tropoelastin: A salt-soluble precursor of elastin. Lysyl oxidase is instrumental in converting it to elastin in connective tissue. [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]

Tuberous Sclerosis: A rare congenital disease in which the essential pathology is the appearance of multiple tumors in the cerebrum and in other organs, such as the heart or

kidneys. [NIH]

Tumor marker: A substance sometimes found in an increased amount in the blood, other body fluids, or tissues and which may mean that a certain type of cancer is in the body. Examples of tumor markers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (prostate cancer). Also called biomarker. [NIH]

Tumor Necrosis Factor: Serum glycoprotein produced by activated macrophages and other mammalian mononuclear leukocytes which has necrotizing activity against tumor cell lines and increases ability to reject tumor transplants. It mimics the action of endotoxin but differs from it. It has a molecular weight of less than 70,000 kDa. [NIH]

Tumour: 1. Swelling, one of the cardinal signs of inflammations; morbid enlargement. 2. A new growth of tissue in which the multiplication of cells is uncontrolled and progressive; called also neoplasm. [EU]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

Ubiquitin: A highly conserved 76 amino acid-protein found in all eukaryotic cells. [NIH]

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]

Univalent: Pertaining to an unpaired chromosome during the zygotene stage of prophase to first metaphase in meiosis. [NIH]

Uraemia: 1. An excess in the blood of urea, creatinine, and other nitrogenous end products of protein and amino acids metabolism; more correctly referred to as azotemia. 2. In current usage the entire constellation of signs and symptoms of chronic renal failure, including nausea, vomiting anorexia, a metallic taste in the mouth, a uraemic odour of the breath, pruritus, uraemic frost on the skin, neuromuscular disorders, pain and twitching in the muscles, hypertension, edema, mental confusion, and acid-base and electrolyte imbalances. [EU]

Urea: A compound (CO(NH2)2), formed in the liver from ammonia produced by the deamination of amino acids. It is the principal end product of protein catabolism and constitutes about one half of the total urinary solids. [NIH]

Uremia: The illness associated with the buildup of urea in the blood because the kidneys are not working effectively. Symptoms include nausea, vomiting, loss of appetite, weakness, and mental confusion. [NIH]

Ureter: One of a pair of thick-walled tubes that transports urine from the kidney pelvis to the bladder. [NIH]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

Uric: A kidney stone that may result from a diet high in animal protein. When the body breaks down this protein, uric acid levels rise and can form stones. [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]

Urokinase: A drug that dissolves blood clots or prevents them from forming. [NIH]

Uterus: The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the womb. [NIH]

Uveitis: An inflammation of part or all of the uvea, the middle (vascular) tunic of the eye, and commonly involving the other tunics (the sclera and cornea, and the retina). [EU]

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]

Vanadium: Vanadium. A metallic element with the atomic symbol V, atomic number 23, and atomic weight 50.94. It is used in the manufacture of vanadium steel. Prolonged exposure can lead to chronic intoxication caused by absorption usually via the lungs. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

Vascular endothelial growth factor: VEGF. A substance made by cells that stimulates new blood vessel formation. [NIH]

Vascular Resistance: An expression of the resistance offered by the systemic arterioles, and to a lesser extent by the capillaries, to the flow of blood. [NIH]

Vasculitis: Inflammation of a blood vessel. [NIH]

Vasoactive: Exerting an effect upon the calibre of blood vessels. [EU]

Vasoconstriction: Narrowing of the blood vessels without anatomic change, for which constriction, pathologic is used. [NIH]

Vasodilator: An agent that widens 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]

Vein: Vessel-carrying blood from various parts of the body to the heart. [NIH]

Venous: Of or pertaining to the veins. [EU]

Venous blood: Blood that has given up its oxygen to the tissues and carries carbon dioxide back for gas exchange. [NIH]

Ventilation: 1. In respiratory physiology, the process of exchange of air between the lungs and the ambient air. Pulmonary ventilation (usually measured in litres per minute) refers to the total exchange, whereas alveolar ventilation refers to the effective ventilation of the alveoli, in which gas exchange with the blood takes place. 2. In psychiatry, verbalization of one's emotional problems. [EU]

Ventilator: A breathing machine that is used to treat respiratory failure by promoting ventilation; also called a respirator. [NIH]

Ventricle: One of the two pumping chambers of the heart. The right ventricle receives oxygen-poor blood from the right atrium and pumps it to the lungs through the pulmonary artery. The left ventricle receives oxygen-rich blood from the left atrium and pumps it to the

body through the aorta. [NIH]

Ventricular: Pertaining to a ventricle. [EU]

Ventricular Dysfunction: A condition in which the ventricles of the heart exhibit a decreased functionality. [NIH]

Ventricular Function: The hemodynamic and electrophysiological action of the ventricles. [NIH]

Venules: The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

Vesicular: 1. Composed of or relating to small, saclike bodies. 2. Pertaining to or made up of vesicles on the skin. [EU]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [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]

Visceral: , from viscus a viscus) pertaining to a viscus. [EU]

Visceral Afferents: The sensory fibers innervating the viscera. [NIH]

Viscosity: A physical property of fluids that determines the internal resistance to shear forces. [EU]

Visual Cortex: Area of the occipital lobe concerned with vision. [NIH]

Visual field: The entire area that can be seen when the eye is forward, including peripheral vision. [NIH]

Vitreous Body: The transparent, semigelatinous substance that fills the cavity behind the crystalline lens of the eye and in front of the retina. It is contained in a thin hyoid membrane and forms about four fifths of the optic globe. [NIH]

Vitro: Descriptive of an event or enzyme reaction under experimental investigation occurring outside a living organism. Parts of an organism or microorganism are used together with artificial substrates and/or conditions. [NIH]

Vivo: Outside of or removed from the body of a living organism. [NIH]

Vocal cord: The vocal folds of the larynx. [NIH]

Weight Gain: Increase in body weight over existing weight. [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]

Xenograft: The cells of one species transplanted to another species. [NIH]

Xenon: A noble gas with the atomic symbol Xe, atomic number 54, and atomic weight 131.30. It is found in the earth's atmosphere and has been used as an anesthetic. [NIH]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [NIH]

X-ray therapy: The use of high-energy radiation from x-rays to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. X-ray therapy is also called radiation therapy, radiotherapy, and irradiation. [NIH]

Yeasts: A general term for single-celled rounded fungi that reproduce by budding. Brewers' and bakers' yeasts are Saccharomyces cerevisiae; therapeutic dried yeast is dried yeast. [NIH]

Zinc Oxide: A mild astringent and topical protectant with some antiseptic action. It is also used in bandages, pastes, ointments, dental cements, and as a sunblock. [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]

INDEX

B

C

N

S

T


9 780597 842061