HYPERLIPIDEMIA

A 3-IN-1 MEDICAL REFERENCE

Medical Dictionary

Bibliography &

Annotated Research Guide

TO INTERNET REFERENCES

ICON Group International, Inc.

HYPERLIPIDEMIA

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

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

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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 hyperlipidemia 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 hyperlipidemia, 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 hyperlipidemia, 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 hyperlipidemia. 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 hyperlipidemia, 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 hyperlipidemia.

The Editors

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

CHAPTER 1. STUDIES ON HYPERLIPIDEMIA

Overview

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

The Combined Health Information Database

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

- **Heightened Gingival Inflammation and Attachment Loss in Type 2 Diabetics with Hyperlipidemia**

  Source: Journal of Periodontology. 70(11): 1313-1321. November 1999.

  Contact: Available from American Academy of Periodontology. Suite 800, 737 North Michigan Avenue, Chicago, IL 60611-2690. (312) 573-3220. Fax (312) 573-3225.

  Summary: Previous studies in rats with diabetes (DB) suggest that **hyperlipidemia** (excessive lipids in the blood) may cause a dysregulation of the cellular and local cytokine response to adult periodontitis (AP). This article reports on a study undertaken to determine if diabetes has a similar dysregulatory effect on the gingival response to AP in humans. Peripheral blood, gingival tissue (GT), and gingival crevicular fluid (GCF), were obtained from a total of 35 patients who were categorized into groups

based on level of diabetes control and presence or absence of AP. All subjects were given a thorough periodontal examination. The results showed that all clinical indices except plaque index were significantly elevated in the poorly controlled and well controlled diabetics, compared to systemically healthy patients, but only in the subjects without preexisting AP. The studies indicated that decreased metabolic control in type 2 diabetes results in increased serum triglycerides and has a negative influence on all clinical measures of periodontal health, particularly in patients without preexisting periodontitis. 1 figure. 4 tables. 49 references.

- **Hearing Improvement After Therapy for Hyperlipidemia in Patients with Chronic-Phase Sudden Deafness**

  Source: Annals of Otology, Rhinology and Laryngology. 110(2): 105-108. February 2001.

  Contact: Available from Annals Publishing Company. 4507 Laclede Avenue, St. Louis, MO 63108.

  Summary: The hearing of patients with chronic phase sudden deafness and associated **hyperlipidemia** (high levels of fats in the blood) tends to improve with therapy for the **hyperlipidemia.** This article reports on a study of 12 patients with unilateral sudden deafness and **hyperlipidemia** in whom more than 1 month had elapsed since the onset of the hearing disturbance. The disturbance was considered to be irreversible without therapy. The 4 men and 8 women ranged in age from 32 to 73 years, with a mean age of 54.3 years. **Hyperlipidemia** was diagnosed when the total blood cholesterol level was 230 mg per dL or greater. The therapy for **hyperlipidemia** consisted of diet therapy and the administration of antilipemic drugs. The hearing level was measured both before therapy and when the total blood cholesterol level had decreased to less than 230 mg per dL. After therapy, the mean hearing level had improved significantly at each of 125, 250, 500, and 2,000 Hertz (Hz), but the changes in the level were not significant at 1,000, 4,000, or 8,000 Hz. The authors conclude that with therapy for **hyperlipidemia,** hearing tends to improve in patients with chronic phase sudden deafness and associated **hyperlipidemia,** even when more than 1 month has elapsed since the onset of the presumably otherwise irreversible hearing loss. 3 figures. 1 table. 8 references.

- **Treatment of Hypercholesterolemia and Combined Hyperlipidemia with Simvastatin and Gemfibrozil in Patients with NIDDM: A Multicenter Comparison Study**

  Source: Diabetes Care. 21(4): 477-481. April 1998.

  Contact: Available from American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 232-3472. Website: www.diabetes.org.

  Summary: This article describes a double-blind, double-dummy study that investigated the lipid-lowering efficacy of simvastatin and gemfibrozil in Finnish patients who had type 2 diabetes and combined **hyperlipidemia** (CHL) or isolated hypercholesterolemia (IHC). Patients with primary dyslipidemia and type 2 diabetes treated with oral hypoglycemic agents and insulin, alone or in combination, were recruited from 10 Finnish centers participating in the study. After a 4-week placebo run-in period, they were randomly assigned to simvastatin or gemfibrozil. The 47 patients in the simvastatin group received 10 milligrams (mg) once a night for 8 weeks, 20 mg for the next 8 weeks, and 40 mg for the third 8-week period. The 49 patients in the gemfibrozil group received 600 mg twice a day throughout the 24 weeks. The lipid-lowering efficacy of both drugs was compared in all patients, as well as separately in patients with CHL and IHC. Results show that simvastatin reduced low density lipoprotein (LDL) and total cholesterol and the LDL-to-high density lipoprotein (HDL) cholesterol ratio more

effectively in all patients, whereas gemfibrozil was more effective in elevating HDL cholesterol and decreasing triglyceride levels. The effects differed according to lipid phenotype at baseline. Simvastatin decreased LDL cholesterol levels by 30 to 40 percent in both phenotypes. Gemfibrozil caused a 15 percent reduction in LDL cholesterol in IHC but no change in CHL patients. Simvastatin produced 15 to 30 percent reductions in triglyceride levels in CHL but no change in IHC patients. Gemfibrozil caused reductions in triglycerides in CHL and in IHC patients, with 12 to 18 percent increases in HDL cholesterol in these groups. The article concludes that simvastatin is useful both in CHL and IHC patients, whereas gemfibrozil can be used in patients with high triglyceride and low or normal LDL cholesterol levels. 1 appendix. 2 figures. 3 tables. 26 references. (AA-M).

- **Hyperlipidemia Therapy in Diabetes**

  Source: Diabetes Educator. 18(2): 105-106, 108-109. March-April 1992.

  Summary: This article reviews the importance of maintaining control of serum lipid levels in people with diabetes to reduce risks for coronary artery disease. Topics include lipid metabolism; lipid handling in diabetes; and therapy for **hyperlipidemia,** including diet, exercise, and drug agents such as bile acid sequestrants, niacin, gemfibrozil, and clofibrate, lovastatin, thyroxine, and probucol. The author focuses on the importance of patient education for better patient compliance and better control of both diabetes and lipids. 2 tables. 1 reference.

- **Transplantation and Hyperlipidemia: What Is It and Why Should I Be Concerned?**

  Source: Stadtlanders Lifetimes. Issue 3: 18-19. 2000.

  Contact: Available from Stadtlanders Lifetimes. Stadtlanders Pharmacy, 600 Penn Center Boulevard, Pittsburgh, PA 15235-5810. E-mail: ltimes@stadtlander.com.

  Summary: This health newsletter article reviews **hyperlipidemia** (increased cholesterol or triglycerides in the blood) and its occurrence in transplant recipients. The author notes that organ preservation, surgical technique, postoperative care, and effective immunosuppressants are improving the life of the transplanted organ, but recipients are still succumbing to cardiovascular illness. **Hyperlipidemia** can occur early after the transplant procedure. Coronary artery disease (CAD), when the arteries supplying the heart become blocked with fatty substances, is the most worrisome effect of **hyperlipidemia.** In addition to some immunosuppressants, other medications that transplant recipients are often prescribed have been known to cause or worsen **hyperlipidemia.** The author stresses the importance of exercise as a way to combat **high cholesterol** levels in the blood. Exercise not only is beneficial on the lipid profile, but also reduces total body weight, strengthens muscle tone, and improves cardiovascular performance. Reducing saturated fat in the diet appears to have the most effect in the overall reduction of cholesterol. For patients whose **hyperlipidemia** is not controlled by at least three months of dietary therapy, treatment with medications should be considered. The author reviews the use of specific drugs (the 'statins') for the treatment of hypercholesterolemia and concerns about rhabdomyloysis (a breakdown of the skeletal muscle tissue, with the inability to clear the breakdown products through the kidney). The author concludes by encouraging readers to educate themselves and to work closely with their transplant team on the appropriate management of **hyperlipidemia.**

Federally Funded Research on Hyperlipidemia

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

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

- **Project Title: A TRANSDERMAL HYPOLIPIDEMIC NIACIN PRODRUG**

  Principal Investigator & Institution: Kim, Hyuntae; Niadyne, Inc. Tucson, Az 85716

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

  Summary: Niacin has been used as first-line drug therapy for elevated serum cholesterol because of its broad efficacy on multiple lipid components as well as its low cost. However, high dose oral formulations of niacin have raised concerns with respect to liver toxicity and unpleasant side effects such as "flushing" that result from the vasodilatory effects of niacin. Consequently, patient compliance with this therapy is problematic. The objective of the research proposed in this application is to determine the feasibility of developing a transdermal delivery form of nicotinic acid for the treatment of **hyperlipidemia** in order to circumvent the side effects associated with its oral administration. Our preliminary results indicate that tissue saturation by niacin via transdermal delivery is feasible and that transdermal delivery via a niacin pro-drug can favorably alter lipid profiles in animal models in animal models. Designing a niacin prodrug with the appropriate physical and chemical properties will allow control of the flux rate through the various layers of skin for the optimum sustained transdermal delivery of niacin. We propose to synthesize and evaluate prodrugs of niacins with formulation properties that will allow sustained delivery of niacin following topical application. We also will compare the effects of oral and transdermal administration of their ability to favorably alter lipid profiles in a double transgenic mouse model that contains lipoprotein profiles similar to the human.

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

- **Project Title: ACCELERATED ATHEROSCLEROSIS IN SLE--PREVALENCE/FACTORS**

  Principal Investigator & Institution: Roman, Mary J.; Professor; Medicine; Weill Medical College of Cornell Univ New York, Ny 10021

  Timing: Fiscal Year 2002; Project Start 01-APR-1999; Project End 31-MAR-2004

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

Summary: (Adapted from the Investigator's Abstract) Autopsy and observational data suggest that systemic lupus erythematosus (SLE) is associated with premature atherosclerosis and myocardial infarction; however, clinical studies have reported widely varying event rates, and the prevalence of underlying disease (atherosclerosis and myocardial disease) in SLE patient samples and its relation to that in a control population are unknown. The prevailing hypothesis has been that accelerated atherosclerosis is attributable to an increased frequency of conventional risk factors in SLE patients such as hypertension, **hyperlipidemia** and obesity, all of which may be provoked or potentiated by therapeutic use of corticosteroids. Alternatively, anti-phospholipid antibody (APLA), present in about 20% of the SLE patients, may result in vascular occlusions due to abnormal clotting rather than atherosclerosis; however, data are accumulating that suggest that the inflammatory process per se may be important in the initiation and progression of atherosclerosis. Pilot data for this study indicate that underlying non-invasively- detected atherosclerosis is several-fold more common in patients with SLE in comparison to matched control subjects. Furthermore, left ventricular mass, a marker for and mediator of enhanced cardiovascular morbidity and mortality, is strikingly higher in SLE patients, even after adjustment for differences in body size. Neither of these observations is explained by standard risk factors. Thus, the goals of this project are to: 1) establish the prevalence of atherosclerosis and myocardial disease in an unselected population of SLE patients; 2) compare findings to those in a control population; 3) determine whether the excess prevalence of pre-clinical cardiovascular disease is independent of known cardiovascular risk factors and is additionally related to markers of inflammation and immune system activation; and 4) determine whether atherosclerosis and LV hypertrophy progress more rapidly in SLE patients than in control subjects. Based on preliminary data, the investigators hypothesize that pre-clinical disease will be more common in SLE and will not be fully explained by conventional risk factors for atherosclerosis or thrombosis. They further hypothesize that basic aspects of the inflammatory process (to be partially investigated using soluble markers in the current project) are primarily responsible for non-valvular cardiovascular disease in SLE.

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

- **Project Title: AGE, LIFESTYLE, MUSCLE MECHANISMS IN INSULIN RESISTANCE**

  Principal Investigator & Institution: Joseph, Lyndon J O.; Medicine; University of Maryland Balt Prof School Baltimore, Md 21201

  Timing: Fiscal Year 2004; Project Start 01-JUN-2004; Project End 31-MAY-2008

  Summary: (provided by applicant): Candidate: Lyndon Joseph, Ph.D., recently joined the faculty as an Assistant Professor in the Division of Gerontology, School of Medicine at the University of Maryland, Baltimore, making this an ideal time to request an MRSDA that will provide the protected research time to learn the molecular techniques necessary to broaden his understanding of whole body insulin action and to determine the cellular mechanism by which weight loss (WL) and aerobic exercise (AEX) improves glucose metabolism in high risk individuals. This will be accomplished via laboratory training, didactic course, and 1:1 mentoring. This training will extend Dr. Joseph's previous education and provide the advanced research skills necessary to launch an independent career in aging research. The long-term career goal of the candidate is to advance academically in a research institution conducting mechanistic research in the study of the pathogenesis of type 2 diabetes with aging and the molecular/cellular effects of exercise and dietary intervention on muscle and glucose metabolism.

Background: Aging is associated with an increase in insulin resistance that may be affected more by obesity and physical inactivity than age per se. Insulin resistance is an underlying abnormality in various metabolic disorders such as type 2 diabetes, **hyperlipidemia,** and hypertension; metabolic diseases that increase cardiovascular morbidity and mortality with aging. Numerous studies show that moderate WL plus AEX improve glucose tolerance and insulin sensitivity in older individuals. However, the molecular and cellular mechanisms underlying these metabolic changes with WL+AEX are not certain. Hypothesis: It is our hypothesis that a lifestyle intervention that incorporates a moderate rate of WL (250-350 kcal/day deficit) plus AEX (70-75% heart rate reserve) will improve glucose tolerance and glucose utilization (80 mU/m2/min hyperinsulinemic-euglycemic clamp) in overweight (25-35 kg/m 2 body mass index), older (60-75 y) glucose intolerant men and women through cellular mechanisms that involve increases in the content, phosphorylation, or activity of intermediates of the insulin-signaling cascade in skeletal muscle (basal and insulin-stimulated muscle biopsies). The specific aim is to determine in-vivo the basal (Glut-4, IRS-1, PI 3-kinase, Akt-kinase protein levels) and insulin stimulated (IR, IRS-1, and CbltCAP phosphorylation, protein kinase C's, PI 3-kinase and AKT-kinase activity) cellular mechanisms in skeletal muscle that may contribute to improvement in glucose utilization after a 6-month WL+AEX program. Environment: The Divisions of Gerontology and Endocrinology, Diabetes and Nutrition at University of Maryland and Department of Physiology, East Carolina University have the resources necessary for my advanced research training in aging, exercise, nutrition, and metabolism research. My mentors, Dr. Goldberg (an investigator in exercise, nutrition and glucose metabolism in aging), and Dr. Dohm (an investigator in cellular and molecular biology of diabetes and obesity) compliment each other in providing me with training to study both whole body and cellular mechanisms of insulin resistance.

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

- **Project Title: AGE-RELATED OBESITY: INTERVENTIONS WITH GENE DELIVERY**

  Principal Investigator & Institution: Scarpace, Philip J.; Pharmacology and Therapeutics; University of Florida Gainesville, Fl 32611

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

  Summary: (provided by applicant): Obesity is the most prevalent nutritional disorder in Western societies. More than three in ten adult Americans weigh at least 20 percent in excess of their ideal body weight. Increased body weight is an important public health problem because it is associated with type II diabetes, hypertension and **hyperlipidemia.** Moreover, adults tend to gain weight as they get older. Our data suggests that the F-344/BN rat is a reasonable model for age-related obesity in humans. These rats demonstrate a steady increase in body fat into early senescence similar to what occurs in humans. Most obese animal models, whether associated with genetic, diet-induced or age-related obesity, display pronounced leptin resistance, rendering leptin treatment futile in treating obesity. Using recombinant adeno-associated virus (rAAV) as a vehicle for long-term leptin gene delivery, our data indicate that leptin, obesity, and age all contribute to the leptin resistance. Furthermore, our data indicate that leptin fails to activate the melanocortin (MC) pathway, and MC agonists are effective in aged-leptin-resistant rats. Our central hypothesis is that impaired activation of the MC pathway characterized by diminished MC tone underlies one mechanism of leptin resistance. We will examine leptin signal transduction in rats made leptin resistant by either chronic leptin treatment or agerelated obesity, whether this results in diminished MC tone, and attempt to circumvent the leptin resistance by gent delivery of

rAAV-POMC, the gene coding for the precursor peptide of cx-MSH. Specifically, this proposal seeks to address three questions in rats of three ages: Does leptin-induced or age-induced leptin resistance result from diminished melanocortin tone. Will silencing of the rAAV-delivered leptin transgene reverse the down-regulated leptin signaling and restore melanocortin tone? Will treatment with rAAVPOMC circumvent leptin resistance and reduce adiposity in leptin resistant rats. Understanding the nature of the leptin resistance is paramount to combating obesity, for only then can we fully exploit the potency of leptin in otherwise leptin-resistant rodents or humans. Such discoveries may lead to new treatments for obesity and the diabetes associated with obesity.

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

- **Project Title: ALCOHOL AS A MODULATOR OF PREFIBROTIC LIVER INJURY**

  Principal Investigator & Institution: Clemens, Mark G.; Professor and Chair; Biology; University of North Carolina Charlotte Office of Research Services Charlotte, Nc 282230001

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 31-JUL-2003

  Summary: Alcohol is implicated as the etiologic agent in greater than 50% of deaths due to liver cirrhosis, a growing national health concern. It is widely accepted that ethanol-induced oxidative injury can result in inflammation, steatohepatitis, hepatocellular carcinoma and fibrosis. However, it is unknown why only a subpopulation of alcoholic liver disease patients present with end stage liver cirrhosis. Likewise, factors contributing to increased obesity-related susceptibility to the deleterious effects of ethanol are poorly understood. This NIAAA R03 has as its primary focus to achieve a basic understanding of whether differences in the severity of alcoholic liver disease can be explained, in part, by alcoholinduced acceleration of preexisting liver injury. This proposal builds on our recent observation that combined hyperlipidemic mice that overexpress apolipoprotein C-I maintained on a chow diet develop prefibrotic liver injury. The hypothesis that will be tested is that alcohol can exacerbate preexisting liver injury initiated by chronic **hyperlipidemia.** In this study, normolipidemic and hyperlipidemic mice fed alcohol or a control diet will be evaluated for changes in plasma lipids and lipoproteins. Intravital microscopy will be used to monitor liver microcirculation, tissue damage and collagen deposition. Tissue evaluation will indicate the metabolic health and extent of liver injury. This study is of immediate interest because while **hyperlipidemia** is pandemic in the US, the observation that chronic **hyperlipidemia** can result in liver injury was previously unappreciated. With our recent observation that chronic **hyperlipidemia** can result in liver injury we will determine whether alcohol can accelerate the development of liver disease in a spontaneous liver injury model where the damage is initiated by preexisting **hyperlipidemia.**

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

- **Project Title: ANGII PROINFLAMMATORY PROCESSES IN ATHEROGENESIS**

  Principal Investigator & Institution: Daugherty, Alan; Professor of Medicine and Physiology; Internal Medicine; University of Kentucky 109 Kinkead Hall Lexington, Ky 40506

  Timing: Fiscal Year 2002; Project Start 20-SEP-2000; Project End 31-JUL-2004

  Summary: (Adapted from Investigator's Abstract): There is evolving evidence for an important role of angiotensin II (AngII) in the atherogenic process. Data derived from clinical trials and animal models using ACE inhibitors indirectly suggests a role for AngII in the atherogenic process; however, the demonstration of a direct role of AngII in

atherosclerosis is still lacking. Preliminary results demonstrate that chronic infusion of AngII promotes rapid development of atherosclerotic lesions and the striking formation of aneurysms in two mouse models of atherogenesis. The central hypothesis of the proposed studies is that AngII interacts with AT1 receptors on macrophages to augment atherogenesis and aneurysm formation by stimulating MCP-1 elaboration and potentiating macrophage and lymphocyte recruitment. To test this hypothesis the PI proposes the following specific aims: 1. Determine the specific AngII receptor responsible for the enhanced atherogenesis and formation of aneurysms using specific antagonists for AT1 or AT2 receptors. 2. Determine the combined effects of **hyperlipidemia** and AngII on the expression of AngII receptors. This will be defined in vivo and in vitro. Quantitative autoradiography will define the expression of distinct AngII receptors in arterial tissue during the evolution of atherosclerotic lesions and aortic aneurysms. These studies will be complemented by studies in cultured macrophages to determine the effects of **hyperlipidemia** and AngII on the regulation of AngII receptors. To link receptor changes to the central working hypothesis, the effect of AngII to release MCP-1 will be determined in vitro in cultured macrophages exposed to hyperlipidemic environments. 3. Determine the macrophage specific contribution of AngII receptor stimulation on the evolution of vascular diseases. This will be achieved by creating chimeric mice in which bone marrow transplantation will be performed to achieve a myeloid cell specific depletion of specific AngII in atherosclerosis susceptible strains. 4. Define the role of MCP-1 in AngII induced atherogenesis and formation of aneurysms. The contribution of AngII induced MCP-1 release to atherogenesis and aneurysm formation will be defined in vivo using mice that are unable to secrete MCP-1 or unable to respond to this cytokine because of deletion of its major receptor, CCR-2. These studies will define mechanisms for AngII augmentation of atherogenesis. Moreover, the development of this animal model for aortic aneurysm formation will allow for definition of mechanisms contributing to this vascular pathology.

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

- **Project Title: ANTIHYPERLIPIDEMIC EFFECTS OF OYSTER MUSHROOMS**

  Principal Investigator & Institution: Abrams, Donald I.; Professor; Medicine; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2003; Project Start 15-SEP-2003; Project End 31-MAY-2005

  Summary: (provided by applicant): Our primary goal is to evaluate the short-term safety and potential efficacy of oyster mushrooms (Pieurotus ostreatus) for treatment of **hyperlipidemia** in HIV-infected patients who are taking ritonavir, a protease inhibitor (PI) that is commonly used in highly active antiretroviral therapy (HAART). While PIs have conferred significant clinical and survival benefits to patients with HIV, some Pls (especially ritonavir) cause **hyperlipidemia** in many patients. Standard treatments for **hyperlipidemia** include the HMG CoA reductase inhibitors or "statins." Unfortunately, many PIs and statins share a common metabolic pathway that uses the CYP3A4 enzyme. Consequently, concomitant administration of ritonavir with most statins increases statin levels significantly, thus increasing the likelihood for adverse effects. Oyster mushrooms have been studied extensively in animal models and have been found to decrease lipid levels - a finding that has been supported by preliminary data in a study in humans. Although these data appear promising, we do not know if oyster mushrooms would have a similar effect in HIV patients with **hyperlipidemia** who are taking a ritonavir-containing HAART regimen. Nor do we know if there is the potential for significant metabolic interactions with ritonavir or whether the concomitant administration of ritonavir and oyster mushrooms increases the likelihood of adverse

effects. We propose to conduct a single-arm, open-label, 8-week "proof of concept" pilot study in 20 subjects to determine if we can detect any lipid-lowering effects of oyster mushrooms in patients with HIV and **hyperlipidemia** who are taking Kaletra (a ritonavir-containing HAART regimen), to assess whether the concomitant administration of oyster mushrooms and such regimens is safe, and to investigate the mechanism of action whereby oyster mushrooms may exert their hyperlipidemic effect. We will test the following 4 hypotheses: (1) Subjects with **hyperlipidemia** will have a reduction in non-HDL-cholesterol during the 8-week pilot study; (2) Oyster mushroom will not alter the hepatic metabolism of Kaletra, thus not increasing its toxicity or decreasing its efficacy; (3) There will be no laboratory or clinical toxicities associated with the daily ingestion of dried oyster mushrooms; and (4) There will be measurable plasma levels of HMG CoA reductase inhibition activity. Data from this pilot study will enable us to determine if further investigation is warranted and, if so, to calculate a sample size for a randomized, controlled trial to evaluate the longer term safety and efficacy of dried oyster mushrooms for treatment of **hyperlipidemia** in this population.

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

- **Project Title: ANTIRETROVIRAL THERAPY AND LONG-TERM CLINICAL OUTCOMES**

  Principal Investigator & Institution: Kitahata, Mari M.; Medicine; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2002; Project Start 01-APR-2000; Project End 31-MAR-2004

  Summary: (adapted from the application s abstract): Recent advances in antiretroviral therapy have dramatically changed the treatment and clinical outcomes for persons with HIV infection. The goal of therapy has expanded from delaying HIV disease progression and death to suppressing viral replication below the level of quantitation for as long as possible to permit immunologic improvement and clinical stabilization. However, now there is a growing proportion of patients who cannot maintain viral suppression often despite changing and more complex therapeutic regimens. The candidate hypothesis s that in the clinic setting, in contrast to the clinical trials setting, a steadily increasing proportion of patients will not have sustained suppression of viral replication over the long-term. Better definition of the generic relationship between longitudinal urologic and immunologic measures and long-term clinical outcomes across the enormous number of antiretroviral combinations available, will become increasingly essential to clinicians. In addition, there is a need to assess potential survival benefits of early and prolonged potent antiretroviral treatment in relation to the long-term effects of treatment-related events, such as neuropathy and metabolic complications (e.g. **hyperlipidemia,** hyperglycemia), on health-related quality-of-life and quality-adjusted survival. To complement and extend information available from clinical efficacy trials, the investigator proposes an epidemiological investigation of predictors of AIDS-free survival and quality-adjusted survival among HIV infected individuals receiving potent combination antiretroviral therapies. For this purpose, she has developed a computerized medical information system at the University of Washington that captures real-time clinical practice information for an HIV clinic population in the Northwest. Collection of comprehensive longitudinal information about HIV infected patients in this clinic setting, may enable the candidate to develop sets of measures of virologic, immunologic, and clinical responses to potent antiretroviral treatment that best predict long-term clinical outcomes. The mentoring and additional training provided by the Mentored Patient-Oriented Research Award will provide the candidate with an opportunity to devote significant efforts to research questions using the clinical

information system and to develop the skills necessary to pursue a research career that blends epidemiological approaches and health services research.

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

- **Project Title: APO B TRANSLOCATION AND DEGRADATION**

  Principal Investigator & Institution: Davis, Roger A.; Professor; Biology; San Diego State University 5250 Campanile Dr San Diego, Ca 92182

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

  Summary: Overproduction of apo B-containing lipoproteins by the liver is responsible for a common form of familial combined **hyperlipidemia** associated with premature cardiovascular disease. Our proposed mechanistic studies in mice will allow us to identify the factors and processes responsible for regulating the secretion of lipoproteins in normal and hyperlipidemic animals and humans. To achieve this goal, we propose the following Specific Aims: 1) To examine the hypothesis that the relative level of expression of MTP and apo B contribute toward determining the maximal capacity of the liver to assemble and secrete apo B-containing lipoproteins. For these studies we will use inbred C57BL/6 mice which have altered expression of MTP and apo B100. 2) To examine the hypothesis that over-production and secretion of apo B-containing lipoproteins is the basis for familial combined **hyperlipidemia.** Using a novel mutant mouse clone displaying a genotype and phenotype that closely reflects a human form of familial combined **hyperlipidemia,** we will determine the molecular basis for this common hyperlipidemic disorder. 3) To define the molecular mechanism responsible for the inactivation of the MTP promoter in L35 cells. L35 cells show a phenotype similar to that of livers from abetalipoproteinemics (i.e. genetic loss of MTP expression and an inability to secrete apo B-containing lipoproteins). We will delineate the mechanism responsible for inactivation of the MTP gene in L35 cells using the promoter constructs that we have shown replicates the transcriptional activity of the endogenous MTP gene. 4) To examine the hypothesis that the relative level of expression of MTP, apo B and lipogenic enzymes displayed by individual liver cells varies dynamically with anatomical localization and changes in physiologic and nutritional state. The knowledge gained from our proposed studies in mice will allow us for the first time to determine the physiologic significance of hypotheses formulated from cultured cell models. New insights gained from these proposed studies should be useful in designing diets and pharmacologic agents that may prevent **hyperlipidemia** and the formation of atherosclerosis in humans.

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

- **Project Title: ATHEROGENESIS AND THE BONE MARROW ANGIOTENSIN SYSTEM**

  Principal Investigator & Institution: Ferrario, Carlos M.; Dewitt Cordell Professor of Surgical Res; Surgical Sciences; Wake Forest University Health Sciences Winston-Salem, Nc 27157

  Timing: Fiscal Year 2002; Project Start 01-SEP-2001; Project End 31-AUG-2005

  Summary: (provided by applicant): Emerging evidence implicates the participation of Ang II in the mechanisms that contribute to early vascular injury, inflammation, and lipid peroxidation, all of which are involved in the initiation of atherogenesis. These investigators hypothesize that production of activated monocytic phenotypes by dyslipidemia is mediated in part by activation of a bone marrow renin-angiotensin system (RAS). Novel features of this hypothesis are: 1) the cells of the bone marrow

produce renin, angiotensinogen, angiotensin-forming enzymes, and angiotensin receptors; 2) dyslipidemia increases bone marrow Ang II production; and 3) production of activated monocytic phenotypes is regulated by increased Ang II type 1 (AT1) receptor expression or activity. In Specific Aim 1, they will investigate the expression of the components of the RAS in cynomolgus monkeys using RT-PCR and Western blot; in addition, they will localize the various components in the cell by a combination of in situ hybridization and immunocytochemistry and assess the type of angiotensin receptors found on hematopoietic cells by flow cytometry. In Specific Aim 2 they will determine the molecular mechanisms by which hyperlipoproteinemia increases bone marrow RAS activity. They will also evaluate the phenotypes of bone marrow cells with flow cytometry and clonogenic assays and identify altered gene expression by array analysis in cynomolgus monkeys fed an atherogenic diet. In Specific Aim 3 they will evaluate whether blockade of the AT1 receptor alters bone marrow myelopoiesis and expression of the bone marrow RAS in hypercholesterolemic cynomolgus monkeys treated with an AT1 receptor antagonist using the techniques listed in Aim 2. The proposed research will uncover novel mechanisms of atherogenesis that may have significant impact in the development of new therapeutic modalities applicable to cardiovascular and blood vessel diseases.

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

- **Project Title: BARIATRIC SURGERY CLINICAL RESEARCH CONSORTIUM**

  Principal Investigator & Institution: Wolfe, Bruce M.; Surgery; University of California Davis Sponsored Programs, 118 Everson Hall Davis, Ca 956165200

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

  Summary: (provided by applicant): A primary objective of obesity research is to define the pathophysiology of obesity as a basis for preventing and/or effectively treating the disease. The areas for research involving bariatric surgery patients may include: 1) defining optimal surgical approaches, 2) identification of biological and genetic differences that influence development of comorbidities and outcomes of surgery, and 3) utilizing this population as a model for study of the pathogenesis and response to treatment of obesity. We propose that the Bariatric Research Clinical Research Consortium (BSCRC) employ a comprehensive relational database that includes parameters readily available to all Clinical Centers (CCs), such as basic anthropometrics, measures of body composition, clinical and surgical history, and recording of a quantitative comorbidity scale. This scale scores each of 17 comorbidities related to obesity, including diabetes, hypertension, and **hyperlipidemia,** and utilizes treatment as a gauge for the severity of symptoms. Further refinement to the comorbidity scale grading may be required by BSCRC participants. This scale will enable comorbidities to be correlated with mRNA expression profiles and endocrine response. UC Davis proposes two specific protocols for conduct by the BSCRC. The short term protocol will measure, using quantitative PCR, the mRNA expression level of obesity related genes in the subcutaneous and omental fat, liver, and intestine of bariatric surgery patients at the time of operation. Measures of body composition including the distribution of body fat, endocrine response to gastric bypass, and the clinical comorbidity scores will allow detailed phenotyping of the subjects from the time of operation to timepoints 2 years post-op. This will be an important initial step towards understanding the variation of comorbidity occurrence between subjects of similar adiposity. The longer term protocol will be a 3-5 year longitudinal study of the response to gastric bypass in relation to hormone activity, body composition, and physical activity. At this phase, correlation with the preoperative genetic and endocrine markers derived in the short term study, as

well as history of comorbidity scores, would identify those patients who would most benefit from gastric bypass. This and other data accumulated by the BSCRC will provide a basis for establishment of further studies of obesity comorbidities and their response to surgical treatment.

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- **Project Title: CELLULAR /MOLECULAR MECHANISMS OF VASCULAR CALCIFICATION**

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

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

  Summary: This Project is focused on understanding the molecular mechanisms involved in vascular calcification and osteoporosis. Matrix GLA protein (MGP) was strongly implicated in the pathogenesis of vascular calcification when an MGP knockout mouse was found to have extensive vascular calcification. Based on this mouse model, MGP might be thought to be an inhibitory factor in vascular calcification. However, in calcified lesions of mice that have a normal MGP gene and in human lesions, MGP expression is postively correlated with the degree of lesion calcification. During the current grant period we demonstrated that MGP regulates bone morphogenetic protein (BMP-2), During the next grant period we will determine the molecular basis for the regulatory role of MGP in the artery wall and its interaction with BMP-2. Other work from this Project during the current grant period provided important clues as to why many patients with progressive vascular calcification also have progressive osteoporosis. Oxidized lipids were shown to promote calcification of calcifying vascular cells (CVC) but inhibited the osteoblastic differentiation and mineralization of marrow stromal cells that are the precursors to mature bone osteoblasts. This was true whether the oxidized lipids were added in vitro or were produced by feeding atherosclerosis suceptible C57BL/6J (BL6) mice an atherogenic diet. These oxidized lipids were also shown to promote osteoclastogenesis and osteoclast activation in vitro. In vivo, feeding an atherogenic diet to atherosclerosis susceptible BL6 mice produced a dramatic reduction in bone mineral density and bone mineral content. Feeding an atherogenic diet to atherosclerosis resistant C3H/HeJ mice causes the same degree of **hyperlipidemia** as in BL6 mice, but there was no significant reduction in either bone mineral density or bone mineral content in the C3H/HeJ mice. In the next grant period we propose to determine the molecular mechanisms for these observations and we will determine if high density lipoproteins (HDL), components of HDL, and mimetics of HDL will protect against bone loss in mouse models of atherosclerosis. These studies may identify potential new therapeutic targets in vascular calcification and osteoporosis.

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

- **Project Title: CLASS B SCAVENGER RECEPTOR, CD36, IN ATHEROSCLEROSIS**

  Principal Investigator & Institution: Febbraio, Maria; Assistant Professor; Medicine; Weill Medical College of Cornell Univ New York, Ny 10021

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

  Summary: (Provided by applicant): CD36 is a broadly expressed transmembrane glycoprotein capable of many functions, including those carried out by scavenger receptors and others, such as adhesion ligand internalization, fatty acid transport and cell signaling. Previous work in our lab demonstrated an important role for CD36 in

atherogenesis: absence of CD36 in the ApoE null background resulted in a 70 percent inhibition of aortic tree lesions. In this application, we will determine the mechanism of atheroprotection afforded by CD36 deficiency by characterizing the role of CD36 in lesion progression. and in models of atherogenesis in which insulin resistance plays a role. We hypothesize that continued progression of lesions may be due to uptake of more extensively oxidized LDL by SR-Al/Il, and we will test this hypothesis by assessment of lesion development in ApoE/CD36/SR-AI/II triple null mice. Alternatively. angiogenesis or efflux may play a role in lesion progression, and we will quantitate vessel number and investigate efflux protein expression. We will characterize the impact of the differential functions of CD36 on atherosclerosis b\ hematopoietic stem cell transplant and conditional cell/tissue ablation of CD36 using CRELox technology. To further investigate the mechanism of atheroprotection in the absence of CD36, we will characterize cholesterol efflux pathways in isolated macrophages from wild type and CD36 null mice, and determine the impact of prior lipid loading, and PPAR-gamma agonists. These studies will be complemented by in vivo assessment of atherosclerotic lesion development after PPAR-y treatment in LDLR/CD36 null and Apo E/CD36 null mice, and in both atherogenic backgrounds after transfer of CD36 stem cells. In this way. the contribution of macrophage CD36 to atherogenesis as compared to fat, endothelial cell and muscle CD36 can be assessed, and specific mechanisms delineated. We believe these approaches will enable us to understand the pathogenesis of foam cell and atheroma development, and lead to novel therapeutic strategies.

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- **Project Title: COMMON MEDIATORS OF VASCULAR CALCIFICATION AND BONE DIS***

  Principal Investigator & Institution: Giachelli, Cecilia M.; Associate Professor; Bioengineering; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-MAY-2005

  Summary: (provided by applicant): Vascular calcification is an actively regulated process contributing to increased morbidity and mortality in, patients with uremia, diabetes, aortic stenosis and bioprosthetic heart valves. Epidemiological studies have linked vascular calcification with osteoporosis and cardiovascular disease, suggesting that common regulatory mechanisms exist, and that ectopic calcification may increase the risk of heart disease. In human blood vessels and valves, both diffuse calcification and ectopic bone have been observed under pathological conditions. The relationship between these types of mineralization is unclear. It is also unknown if media or intimal vascular calcification contributes to formation and/or progression of atherosclerotic lesions. We hypothesize that mineral deposition in blood vessels involves mediators including osteopontin (OPN), osteoprotegerin (OPG) and matrix gla proteins (MGP), that also critically control formation of the skeleton, and that once mineral forms in the vessel wall, an adaptive response ensues and initiates cellular differentiation and inflammatory mechanisms that 1) lead to neointima formation and hence increased susceptibility to plaque formation, and 2) mimic endochondral bone formation that may explain the appearance of ectopic bones in calcified vascular lesions. In order to identify common mechanisms! controlling bone and vascular calcification, and to understand the relationship between vascular calcification, cartilaginous metaplasia, and arterial lesion development, three aims are proposed. Aim I will determine the mechanism of medial vascular calcification, neointimal formation, and cartilaginous metaplasia in MGP X OPN mutant mice. Aim 2 will determine the mechanism of bone and tooth defects

found in MGP X OPN mice. Aim 3 will determine the effect of **hyperlipidemia** on cartilaginous metaplasia, vascular calcification and osteoporosis in a mouse model of atherosclerosis.

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- **Project Title: DESIGN AND SYNTHESIS OF NONPEPTIDE PROTEASE INHIBITORS**

  Principal Investigator & Institution: Ghosh, Arun K.; Associate Professor; Chemistry; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2002; Project Start 01-SEP-1995; Project End 31-AUG-2006

  Summary: (provided by applicant): HIV protease inhibitors in combination with reverse transcriptase inhibitors continue to be first line antiviral agents for control of HIV infection. While protease inhibitors are most useful in the treatment of AIDS, there are serious limitations including major toxicity, complexity, and perhaps the most serious of all, the emergence of mutidrug resistant strains of HIV. There is now ample evidence that these strains can be transmitted. In addition, tolerance and adherence to complex medical regimens are becoming a critical issue. The drugs must be taken in gram quantities daily because of low oral bioavailability. Most currently approved protease inhibitors (PIs) are associated with complex side effects including peripheral lipodystrophy, **hyperlipidemia** and insulin resistance. In this context, our current research emphasis has been to design and synthesize nonpeptidyl protease inhibitors and optimize their potency against mutant strains resistant to the currently approved protease inhibitors. We recently developed a number of novel nonpeptidyl HIV protease inhibitors based upon X-ray structures of the protein-ligand complexes. One of these inhibitors is currently undergoing clinical trials at Tibotec -Virco in Belgium. Based upon X-ray structures of our inhibitors, we have generated a number of interesting small molecule leads. This work now forms the basis of our proposed studies in which the power of crystallography and molecular modeling will be utilized to further develop a new generation of nonpepfidyl protease inhibitors with improved pharmacological and resistance profiles. Our specific aims of the present proposal are: (a) to perform structure-activity studies of lead small molecule inhibitors; (b) to further optimize the potent inhibitors' resistance profiles based upon crystallographic information; (c) to design and synthesize novel nonpeptidyl inhibitors incorporating novel designed ligands and templates; (d) to incorporate functionalities for combating drug resistance and improving oral absorption poperties; (e) to conduct in-depth resistance profile s to further optimize inhibitors. Our proposed research effort will involve the realms of organic synthesis, medicinal chemistry, biochemistry, molecular biology, protein ligand X-ray crystallography and molecular modeling. Besides the broad range of scope and generality, this line of research will provide excellent opportunities to teach and train students in the laboratory.

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- **Project Title: DIABETIC NEUROPATHY: IMPLICATIONS FOR WOUND REPAIR**

  Principal Investigator & Institution: Gibran, Nicole Simone.; Associate Professor; Surgery; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2003; Project Start 30-SEP-1999; Project End 31-AUG-2007

  Summary: (provided by applicant): This proposal explores cell signaling pathways that occur between cutaneous sensory nerve fibers and endothelial cells in response to cutaneous injury. Our previous data suggest that nerve-derived neuropeptides

contribute to the normal wound repair process. In contrast, non-healing chronic ulcers associated with diabetes mellitus are characterized by microangiopathy and decreased innervations. Based on encouraging data during the past funding period we continue to explore our hypothesis that in patients with diabetes mellitus, hyperglycemia and **hyperlipidemia** impair microvascular endothelial cell response to nerve-derived neuropeptides and endothelial cell production of necessary inflammatory mediators. These abnormalities contribute to impaired response to cutaneous injury. We will test our hypothesis by addressing the following Aims: Aim 1: To determine the effects of hyperglycemia and matrix glycosylation on microvascular endothelial cells responses. Hyperglycemia can directly alter cellular responses and can indirectly alter cellular response by extracellular matrix molecule glycosylation. We will determine whether hyperglycemia and/or matrix molecule glycosylation alters SP-induced endothelial cell mediator synthesis, cytoskeleton organization, integrin expression and intracellular signaling. Aim 2: To determine the effect of elevated fatty acid levels on endothelial cell responses. **Hyperlipidemia** is strongly associated with complications in diabetes mellitus. We will determine whether elevated fatty acids alone or as Triglycerides alter SP-induced endothelial cell mediator synthesis, cytoskeleton organization, integrin expression or intracellular signaling. Aim 3: To determine the anti-oxidant regulation of microvascular endothelial cell response to hyperglycemia & **hyperlipidemia.** Oxidative stress due to **hyperlipidemia** may alter cellular response to injury. We will continue our studies of effects of antioxidants, vitamin E, vitamin C and n-acetyl cysteine on cellular responses under hyperlipidemic and hyperglycemic conditions. Aim 4: To determine whether restoration of neuropeptide activity improves wound repair in diabetic mice. We will use several approaches to evaluate the roles of neuropeptides in wound repair. Using an excisional wound repair model in hyperglycemic db/db mice, we will replace substance P and inhibit neutral endopeptidases activity. We will also test the effects of antioxidants in this murine wound model.

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- **Project Title: DIET, ENDOTHELIAL FUNCTION AND PEDIATRIC HYPERLIPIDEMIA**

  Principal Investigator & Institution: Engler, Marguerite M.; Physiological Nursing; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002; Project Start 01-APR-2000; Project End 31-DEC-2004

  Summary: Coronary heart disease (CHD) remains the leading cause of death in the United States. The pathogenesis of atherosclerosis and CHD is thought to be initiated by endothelial dysfunction or injury. Factors that contribute to oxidative stress such as elevated cholesterol-rich low density and very low-density lipoproteins (LDL and VLDL) result in endothelial dysfunction. The long term goal of this proposal is to develop dietary interventions for the prevention and treatment of endothelial dysfunction in children and adolescents who are at high risk for premature CHD due to the genetic lipid disorders of familial hypercholesterolemia (FH) or familial combined **hyperlipidemia** (FCH). This experimental, randomized, double blind crossover, placebo-controlled clinical trial will include 96 hyperlipidemic children and adolescents aged 10 to 18 years who will receive dietary supplements and an intensive dietary educational program. The following hypothesis will be evaluated: Specific nutrients in the diet will have direct beneficial vascular effects and/or indirect effects on lipoprotein composition which will in turn decrease the oxidation of LDL and the level of vascular oxidative stress, thereby improving endothelial function. The primary specific aims are: 1) to determine whether a National Cholesterol Education Program (NCEP) Step II diet

alone or together with one of four putative vasculoprotective supplements (Vitamins C & E, w-3 fatty acids, L-arginine, folic acid) will improve endothelial function in children and adolescents with FH and FCH, and 2) to evaluate the effects of these supplements on plasma lipoprotein profiles, LDL composition, lipoprotein-associated antioxidant enzymes (paraoxonase and platelet activating factor acetyl hydrolase), indices of oxidative stress (oxidized LDL, 8-hydroxy-2'-deoxyguanosine), immune function (inflammatory cytokines, plasma adhesion molecules), and blood pressure. Vascular reactivity, a sensitive indicator of endothelial function, will be measured noninvasively using high-resolution external vascular ultrasound of the brachial artery. The secondary aims are: 1) to examine children and adolescents psychological well being, beliefs and feelings about their cardiovascular status and its relation to health outcomes, and 2) To explore their practices and health risk behaviors specifically in the area of dietary adherence. These studies will provide important insight into the mechanism of endothelial dysfunction and should serve to identify potential treatments for pediatric **hyperlipidemia.** Preventive nursing strategies aimed at early detection of endothelial dysfunction and dietary modification may restore endothelial function in children and adolescents at high risk for CHD.

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- **Project Title: DIETARY ADHERENCE IN CHILDREN WITH CHRONIC CONDITIONS**

  Principal Investigator & Institution: Ievers-Landis, Carolyn E.; Pediatrics; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

  Timing: Fiscal Year 2002; Project Start 11-JUN-2001; Project End 31-MAY-2006

  Summary: (Adapted from applicant's description): The candidate is a research associate in pediatric psychology who is advancing to a junior faculty position. This award is expected to help transition the focus of the candidate's research and provide additional training in measurement of dietary adherence, particularly of barriers associated with following prescribed diets for children with various chronic conditions. The candidate's career goals are to develop an independent research career related to elucidation of barriers and family interaction patterns that interfere with dietary adherence and development of intervention programs to promote adherence. Specific objectives are: 1) learn specialized methods of measurement to identify the challenges related to the dietary management of chronic conditions of childhood, including in-depth interviews and behavioral analyses of family interactions at mealtimes, and 2) use data from these methods to develop family-based interventions to promote adherence to dietary regimens. The candidate proposes a five-year training program with faculty mentors from a strong pediatric research department and medical school. Her sponsor is a very experienced pediatric psychology researcher whose work has focused on identifying factors that enhance or disrupt the psychosocial adaptation of children with chronic illness. Mentors represent subspecialty divisions that are directly relevant to the research and career development plan. The career development plan describes activities focused on enhancing knowledge of research-related approaches to the identification of barriers to dietary adherence and design of intervention programs through clinical observation, course work, and independent studies with mentors. Other activities include research training in statistical methods and supervised experience in preparation of grant proposals for individual research support. The candidate's proposed research involves two studies. Study 1 is a two-phase assessment of barriers to dietary adherence in children with **hyperlipidemia,** insulin-dependent diabetes mellitus, phenylketonuria, and Prader-Willi syndrome. Study 2 is a pilot study to

develop and evaluate family-based intervention programs to improve dietary adherence for children in the target populations.

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- **Project Title: DIETARY GLYCEMIC LOAD, BODY WEIGHT, AND BLOOD LIPIDS**

  Principal Investigator & Institution: Ma, Yunsheng; Medicine; Univ of Massachusetts Med Sch Worcester Office of Research Funding Worcester, Ma 01655

  Timing: Fiscal Year 2004; Project Start 01-APR-2004; Project End 31-MAR-2006

  Summary: (provided by applicant): The overall goal of this 2 year proposal is to examine the association of glycemic load (GL), derived from 24-hour dietary recalls, with body weight and blood lipids (including total cholesterol, LDL, HDL, and triglycerides), and to study seasonal and short-term variation of GL in a free-living healthy population. Results from short-term experimental studies and a limited number of observational studies suggest that GL, a measure of the quality and quantity of carbohydrate in foods, may be related to body weight and serum lipids, and GL potentially should be considered in dietary recommendations. However, neither the glycemic index (GI) nor GL is considered in the dietary guidelines of the American Heart Association, the U.S Department of Agriculture, or the American Diabetes Association. We will use dietary data collected from the Seasonal Variation in Blood Cholesterol Levels (SEASONS) (NHLBI: R01-HL52745) (1. Ockene - P.I.) study, in which 641 healthy adults in central Massachusetts were followed quarterly (baseline and four consecutive quarters: five sampling points in all) during this a one-year observational study. A total of fifteen 24-hour dietary and physical activity recalls were collected for each subject, with serum lipids and body weight measured five times. Serum lipids and body weight were measured once per quarter and three 24-hour recalls were administered (two weekdays and one weekend day) per quarter. If GL is found to be associated with body weight and blood lipids, a randomized clinical trial will be designed to evaluate the effects of a GL-based nutritional intervention program on hyperlipidemic patients. The methodology of this proposed study will involve several steps: 1) Data summarization of 9,067 24- hour diet recall records, 2) GL calculation and calculation of overall GI index, 3) Analysis of the relationship of GL to body weight and blood lipids, 4) Estimation of seasonal and short-term variations in GL, 5) Analysis of GL by meal type and identification of the top ten food contributors, 6) Analysis of the association of overall GI with body weight and blood lipids, and 7) Final report and manuscript preparation.

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- **Project Title: DISLIPIDEMIA DETECTION IN WV FAMILIES**

  Principal Investigator & Institution: Harris, Carole V.; Behavioral Med and Psychiatry; West Virginia University P. O. Box 6845 Morgantown, Wv 265066845

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

  Summary: (provided by applicant): West Virginians are at high-risk for developing coronary heart disease due to high rates of biomedical risk factors, low socio economic status, and a rural geography with limited access to health care. West Virginian's health beliefs influence participation in health care programs and must be considered in the development of interventions to improve health. The long-range goal of this research program is to prevent the development and progression of coronary heart disease in at-risk children and their parents. The objective for this application is to identify and reduce the health belief barriers to an existing cholesterol screening program in this

high-risk, rural, poor population. The existing program, Coronary Artery Risk Detection in Appalachian Communities (CARDIAC) has a four year history of providing no cost dyslipidemia testing to fifth grade children and their parents. The specific aims for this proposal are: (1) To identify health beliefs that act as barriers to participation in the dyslipidemia screening program and to develop belief-based strategies to reduce those barriers, and (2) To improve the identification of children and families who are at-risk for the development of CHD. Research Design and Methods: The Theory of Planned Behavior will provide the theoretical framework for identifying beliefs barriers and developing interventions to address them. Belief barriers to participation in the dyslipidemia detection program will be initially identified through interviews with children, parents, and community leaders in rural West Virginia. The reliability and validity of interview responses will be assessed through administration of general and study-specific health beliefs questionnaires to a larger, random sample of children and adults. A Health Beliefs (HB) approach will be developed for the screening and diagnosis phases of the dyslipidemia detection program. The new HB approach will be compared to the standard CARDIAC (SC) approach in a randomized controlled trial. Three thousand fifth grade students in fourteen counties will be randomly assigned to receive either the HB or SC approach. Participants will be followed through screening and diagnosis. The HB and SC approaches will be compared on participation rates for children and parents.

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- **Project Title: DTC ADVERTISING EFFECT ON ADHERENCE TO STATIN THERAPY**

  Principal Investigator & Institution: Bradford, W D.; Associate Professor; None; Medical University of South Carolina P O Box 250854 Charleston, Sc 29425

  Timing: Fiscal Year 2004; Project Start 01-JUL-2004; Project End 31-MAY-2007

  Summary: (provided by applicant): In August of 1997 the Food and Drug Administration (FDA) relaxed the rules governing broadcast advertising of prescription pharmaceutical products. Shortly thereafter, expenditures on direct to consumer advertising (DTCA) for prescription pharmaceuticals soared. This has lead to a great deal of debate in the medical profession and among health care insurers and managed care organizations. We propose to study one possible effect of DTCA - whether exposure to DTCA can improve patient adherence to prescribe pharmaceutical therapy (statins) for the treatment of **hyperlipidemia.** Adherence to therapy is known to be a barrier to effective care for many chronic diseases. Treatment with prescription statins has become a principal modality for managing **hyperlipidemia.** Several of the statins are among the most heavily advertised pharmaceuticals since 1997. We hypothesize that patients who are in areas where these drugs are heavily advertised will have better adherence to their prescription therapy than patients who live in areas where these drugs are not advertised, and as a consequence will have better outcomes. This proposal has four principle aims: 1) determine the degree to which DTCA affects physician patient populations; 2) determine the impact of DTCA on the likelihood that a patient is prescribed a lipid-lowering drug; 3) determine the impact of DTCA on adherence to therapy, given that a patient has a prescription; and 4) Determine the impact of DTCA on the effectiveness of prescription statin therapy. This study will utilize a unique research data base which combines detailed clinical information (from an extract of the electronic medical records of 65 geographically dispersed primary care practices) with detailed advertising data (brand, month, and media-market specific). A series of

econometric models will be estimated to determine the adherence and health effects of DTCA.

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

- **Project Title: DYSREGULATION OF GLUCOSE HOMEOSTASIS IN AGING**

  Principal Investigator & Institution: Barzilai, Nir J.; Director: Institute for Aging Research; Medicine; Yeshiva University 500 W 185Th St New York, Ny 10033

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

  Summary: In this project, we propose to continue our investigation of the biochemical and molecular mechanism(s) by which the regulation of glucose metabolism fails with aging. Such dysregulation is associated with impairments in insulin action on the muscle and liver, and a decreased ability to secrete insulin by the beta- cells of the pancreas. An increase in visceral/abdominal fat, more so than a general increase in fat mass, is a specific risk factor for a variety of conditions such as **hyperlipidemia,** hypertension and diabetes, resulting in increased cardio-vascular mortality with aging. We have previously characterized aging animal models that exhibit some of the metabolic features of human aging, and demonstrated a major cause/effect relationship between age-related changes in body composition and the impairment in hepatic and peripheral insulin action. Interestingly, longevity is increased in caloric restricted animal models, supporting the notion that fat mass has deleterious effects leading to mortality. Recently we discovered that the fat-derived peptide leptin regulates body fat distribution, in addition to its effect to increasing insulin action. We hypothesize that the typical increase in visceral/abdominal fat determines the impairment in glucose metabolism seen in aging. Furthermore, we suggest that aging is an "leptin resistance" state, in which leptin fails to regulate body fat distribution and to maintain insulin action. We will test this hypothesis by preventing the increase in visceral/abdominal fat in rodents by caloric restriction or surgical removal of the visceral fat. We will study whether the age-related impairments in the molecular physiology of peripheral and hepatic insulin action, and in insulin secretion are thereby averted. Furthermore, we will determine if chronic leptin administration to aging rats will fail to regulate body fat distribution and insulin action. The effect of the changes induced in body composition on glucose metabolism, will be determined in vivo, and muscle, liver and pancreatic tissue will be analyzed to determine the relevant substrates, enzyme activities, and gene expressions after acute manipulations. This proposal is significant for determining the causal role that visceral fat has on the impaired glucose metabolism in aging, and the potential cause for this phenomenon. Once mechanisms for dysregulation of glucose metabolism are identified in animal models, interventions specifically designed to alter body composition in human aging may be proposed.

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

- **Project Title: EFFECT OF PF4 ON LIPOPROTEIN METABOLISM/ATHEROSCLEROSIS**

  Principal Investigator & Institution: Sachais, Bruce S.; Assistant Professor; Pathology and Lab Medicine; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2002; Project Start 15-JAN-2000; Project End 31-DEC-2004

  Summary: (Adapted from applicant's abstract) Atherosclerosis is the most common cause of death in the United States. Elevated plasma levels of LDL are a major risk factor for the development of this disease. The major pathway by which LDL is catabolized is

via the LDL-receptor (LDL-R). Therefore, factors that impede LDL-LDL-R interactions promote atherosclerosis. An unexplored question is whether platelet activation modulates LDL-R function. Whereas the role of platelets in the terminal thrombotic phase of this disease is well- established, it is less certain whether persistent platelet activation accelerates the pathogenesis of the atherosclerotic plaque. In view of the fact that certain clusters of positively charged residues on apolipoprotein Beta-100 are required for optimal binding of LDL to the LDL-R, the investigators tested the hypothesis that platelet factor 4 (PF4], an abundant lysine rich protein released upon platelet activation, can complete for receptor binding and thereby impede lipoprotein clearance and catabolism. Pilot data provided support for this hypothesis by demonstrating that PF4 binds to the LDL-R with nM affinity, inhibits the binding and degradation of LDL in vitro, and prolongs the plasma clearance of LDL in vivo. It is now proposed to study the biochemicals basis of the PF4-LDL-R interaction in greater detail and to develop models to elucidate the role of this platelet protein in the development of atherosclerosis through the following specific aims; 1) Specific Aim 1: Characterization of PF4 binding to the LDL-R and it's consequences in vitro. The binding kinetics of PF4 to cell lines that overexpress LDL-R as well as to recombinant soluble receptor will be measured using surface plasmon resonance. The effect of PF4 on the binding and cellular metabolism of LDL and apoE will be studied using cells that are genetically lacking or overexpress LDL-R and in which the level of proteoglycan expression has been controlled. Specific Aim 2: Effect of PF4 on lipoprotein metabolism and atherosclerosis in vivo. Adenoviral-mediated gene transfer of PF4 will be used to analyze changes in LDL clearance and endogenous lipoprotein levels in vivo. The propensity to develop **hyperlipidemia** and atherosclerosis will be examined in transgenic mice that overexpress human PF4. These studies are designed to gain insight into a novel mechanism by which persistent platelet activation may promote the development of atherothrombotic disease. An understanding of the structural basis of the PF4-LDL-R interaction may identify a potential locus for therapeutic intervention. This research proposal is part of comprehensive training program designed to prepare the applicant for a career as an independent investigator in the field of vascular biology.

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- **Project Title: ENDOTHELIAL DYSFUNCTION DUE TO HIV-1 PROTEASE INHIBITORS**

  Principal Investigator & Institution: Dube, Michael P.; Medicine; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, in 462025167

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-JUL-2007

  Summary: (provided by applicant): HIV-1 protease inhibitor (PI) agents have revolutionized HIV care, but have led to marked abnormalities in metabolism. These changes appear to place patients with HIV infection at considerably increased cardiovascular risk. In addition to insulin resistance and **hyperlipidemia,** endothelial dysfunction occurs and will heighten these risks. Endothelial dysfunction is a critical initial step of atherogenesis that subsequently contributes to the progression and clinical manifestations of atherosclerosis. Preliminary data show that the PI indinavir impairs endothelium-dependent, nitric oxide-mediated, vasodilation in normal subjects. To further define the factors contributing to endothelial dysfunction, identify antiretroviral agents with lesser cardiovascular risk, and identify potential interventions, this project addresses these Specific Aims: (1) Establish the physiologic mediators of endothelial dysfunction caused by indinavir: The hypothesis that insulin resistance mediates endothelial dysfunction due to indinavir will be tested. Normal subjects will receive

indinavir for 4 weeks and undergo measurements of endothelium-dependent vasodilatory response both before and during hyperinsulinemia. (2) Compare the effects of PIs with divergent metabolic effects on endothelial function: To test the hypothesis that PIs with lesser tendencies to provoke insulin resistance or dyslipidemia will have lesser effects on endothelial function, normal subjects will be randomized to receive either amprenavir or atazanavir. Similar tests of endothelial function will be performed. (3) Determine if non PI-based combination therapy results in less endothelial dysfunction than a PI-based regimen. The hypothesis that a PI-based antiretroviral combination regimen will induce endothelial dysfunction, but a non-PI-based regimen will not, will be tested. HIV-infected subjects will be randomized to a PI-based regimen that is expected to cause dyslipidemia and insulin resistance, or a non-PI-based regimen that should not. Subjects will cross over to the other therapy after 12 weeks of treatment to establish the reversibility of the endothelial dysfunction. The results of these studies will provide a better understanding of the causes of increased cardiovascular risk among HIV-infected patients, foster the development of antiretroviral drugs that lack adverse effects on cardiovascular risk, and identify potential interventions to test for reduction of risks in HIV-infected patients.

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- **Project Title: GENERATING MOUSE MUTANTS WITH DIABETIC NEPHROPATHY**

  Principal Investigator & Institution: Breyer, Matthew D.; Professor; Medicine; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-AUG-2006

  Summary: (Provided by Applicant): Diabetic nephropathy (DN) is a disease of monumental proportions both in terms of human suffering and public health expenditures. Approximately six percent of the U.S. population has diabetes mellitus, 10-20% of which develop DN, ultimately progressing to end stage renal disease (ESRD). The factors contributing to DN remain obscure. While hyperglycemia is a necessary trigger, alone, it is insufficient to cause DN. Sibling studies suggest a strong genetic component, however defining the specific genetic loci contributing to DN in man has been confounded by the heterogeneous causes of diabetes, and by the diversity of human genetic background. In contrast, the wide availability of genetically homogenous mouse strains, coupled with advances in transgenic technology, make mice uniquely amenable to dissection of the molecular mechanisms of disease. As in man, most mice do not develop diabetic nephropathy, and the array of genes that confer susceptibility to DN to this minority, have not been characterized. This proposal is to generate a robust murine model of DN that closely parallels the human disease; that is genetically defined; and can be easily transferred between mouse strains. To achieve these goals we propose to identify specific genes that convert the "nephropathy resistant" C57BL/6 strain to one that develops DN. We will take two approaches. The first will use a "candidate gene" approach. In man, patients susceptible to DN exhibit worse hypertension and dyslipidemia than those resistant to nephropathy. Treatment of these conditions slows the progression of nephropathy. Polymorphisms in Angiotensinogen (Atg) eNOS and ApoE alleles have been described in susceptible patients. The first specific aim will examine the effect of superimposing the hypertensive human Atg transgenic, eNOS-/- or hyperlipidemic ApoE-/- alleles on two different models of diabetes, insulin deficient HN6 transgenic mice and insulin resistant db/db mice. The second approach will attempt to identify novel dominant modifiers that predispose to DN. Diabetic HNF6 or db/db C57BL/6 mice will be mutagenized with ethylnitrosourea (ENU) and G 1

offspring screened for DN (renal insufficiency and/or proteinuria). These studies should not only yield a well-defined mouse model of DN, but also provide important new information regarding genes that contribute to the development of DN.

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- **Project Title: GENETIC DETERMINANTS: LOW HDL, HIGH TRIGLYCERIDES, OBES***

  Principal Investigator & Institution: Mahley, Robert W.; Director; J. David Gladstone Institutes Box 419100, 365 Vermont St San Francisco, Ca 94103

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

  Summary: (provided by applicant): Over the past 10 years, extensive studies have been conducted in Turkey to determine the risk factors for heart disease. Studies involving approximately 10,000 Turkish men and women from six different regions of Turkey have established that this population is unique in several ways. The Turks have the lowest plasma levels of high density lipoprotein cholesterol (HDL-C) of almost any population in the world (75 percent of the men and 50 percent of the women have HDL-C levels 30 kg/M2], and both men and women have a tendency toward hypertriglyceridemia. The low HDL-C, however, is independent of obesity or hypertriglyceridemia. Samples from this well-characterized population provide a unique opportunity to explore the genetic determinants associated with the high prevalence of low HDL-C, hypertriglyceridemia, and obesity (characteristics of the metabolic syndrome). This project will analyze DNA from frozen blood samples to investigate new candidate gene targets that may provide insights into the abnormalities characterizing this population. The samples and extensive biodata are available on all 10,000 participants. In Specific Aim 1, we will identify polymorphisms in acyl CoA:diacylglycerol acyltranferase (DGAT)- I and -2 and in ATP-binding cassette A I (ABCA I) genes that are associated with differences in BMI, HDL-C, and triglyceride concentration, and other parameters such as blood pressure. These studies will focus significantly on promoter and coding sequence polymorphisms in DGAT-I and -2 and ABCAL In Specific Aim 2, we will determine whether the polymorphisms have functional significance by using a luciferase reporter system to determine expression of polymorphic forms of DGAT and ABCAI, a cholesterol efflux measurement to determine the functional significance of ABCAI coding sequence polymorphic sites, and a triglyceride synthesis assay to determine the functional significance of DGAT-I and -2 polymorphic sites. The polymorphic site association studies will be performed on DNA samples from three subgroups of Turks: (a) individuals likely to have the metabolic syndrome, (b) individuals with isolated low HDL-C (normal triglycerides), and (c) normolipidemic unaffected controls.

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- **Project Title: GLYCATION OF PROTEIN IN DIABETES**

  Principal Investigator & Institution: Baynes, John W.; Professor; Chemistry and Biochemistry; University of South Carolina at Columbia Byrnes Bldg., Room 501 Columbia, Sc 29208

  Timing: Fiscal Year 2002; Project Start 01-AUG-1977; Project End 31-JUL-2007

  Summary: (provided by applicant): This research program addresses the hypothesis that damage to proteins and other biomolecules by nonenzymatic glycation and Maillard or browning reactions contributes to the pathogenesis of the long-term complications of diabetes. The proposed mechanism involves formation of irreversible advanced

glycation and lipoxidation end-products (AGE/ALEs) that affect protein structure and function and alter metabolism in tissues in which complication develop. We have tested the Maillard hypothesis by evaluating the effects of AGE/ALE inhibitors on the chemical modification of proteins and development of complications in animal models of diabetes, including the streptozotocin-diabetic and Zucker obese rat These studies have raised questions about the effects of AGE/ALE inhibitors on enzymatic crosslinking of proteins, have led to the identification of a new class of AGE/ALEs derived from cysteine, and have yielded insight into the carbonyl trapping activity and mechanism of action of the AGE/ALE inhibitor pyridoxamine (PM). During the continuation period of this grant, our Specific Aims are: 1) to evaluate the effects of diabetes, **hyperlipidemia** and AGE/ALE inhibitors on the formation of enzymatic, as well as nonenzymatic, chemical modifications and crosslinks in collagen, including studies on the chelating activity of AGE/ALE inhibitors in vivo; 2) to study the formation and biological significance of Cys-AGE/ALEs in diabetes and **hyperlipidemia,** including basic research on the reaction of protein sulfhydryl groups with glyoxal, methylglyoxal and fumarate, comparison of levels of Cys-AGE/ALEs in intracellular and extracellular proteins, effects of treatment with AGE/ALE-inhibitors, identification of major intracellular proteins modified by Cys-AGE/ALEs, and evaluation of the regulatory significance of Cys-AGE/ALE formation; 3) to continue studies on PM in order to identify reactive intermediates trapped by this compound in vitro and in vivo, to evaluate effects of PM on levels of dicarbonyl intermediates in plasma, and to evaluate the effects of PM on AGE/ALE formation and development of pathology in a non-hyperlipidemic animal model, the diabetes prone BB/Wor rat. Through this work, we hope to gain a better understanding of the role of AGE/ALEs in the pathogenesis of diabetic complication and the mechanism of action of AGE/ALE inhibitors, leading eventually to the development of more effective therapies for treatment of diabetes and its complications.

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- **Project Title: GORDON RESEARCH CONFERENCE ON LIPOPROTEIN METABOLISM**

  Principal Investigator & Institution: Phillips, Michael C.; Professor; Gordon Research Conferences Box 984, 512 Liberty Ln West Kingston, Ri 028920984

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

  Summary: (provided by applicant): This application is for partial support of the 2002 Gordon Research Conference on Lipoprotein Metabolism to be held at Kimball Union Academy in Meriden, New Hampshire on June 16-21, 2002. The title of the conference is "Molecular Mechanisms and Regulation of Lipoprotein Metabolism." This international conference will focus on important new developments in lipoprotein metabolism, particularly in those areas that impact on human metabolic disease and the development of atherosclerotic vascular disease. Basic molecular and cell biological studies and in vivo studies in humans and animal models will be presented. Topics will include high density lipoprotein metabolism, cholesterol transport, insulin resistance, nuclear receptors, and the application of genomics. Nine sessions are planned and will cover: 1. HDL Apolipoprotein Structure-Function 2. Genetics and In Vivo Regulation of HDL Metabolism and Reverse Cholesterol Transport 3. Niemann Pick C Disease and Intracellular Trafficking of Cholesterol 4. Reverse Cholesterol Transport 5. Insulin Resistance and **Hyperlipidemia** 6. Nuclear Receptors and Lipoprotein Metabolism 7. Lipid Metabolism in the Brain 8. Genomics and the Study of Lipid Metabolism 9. Keynote Speaker: H. Bryan Brewer This conference will be a major vehicle for the

presentation and integration of the latest developments in lipoprotein and lipid metabolism. Emphasis will be placed on in-depth presentations and thorough discussions of new, largely unpublished studies. Important aims of the Gordon Research Conference on Lipoprotein Metabolism are to include the diversity of qualified professionals and to foster interactions among young investigators, post-doctoral fellows, graduate students, and senior investigators.

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- **Project Title: HEART DISEASE IN RHEUMATOID ARTHRITIS**

  Principal Investigator & Institution: Gabriel, Sherine E.; Professor; Mayo Clinic Coll of Medicine, Rochester 200 1St St Sw Rochester, Mn 55905

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

  Summary: (Applicant's Abstract) The hypotheses to be tested in this proposal are built on findings from two intriguing, but rather disparate lines of investigation. The first is the recent data suggesting that the excess mortality experienced by people with rheumatoid arthritis (RA) may result from increased rates of coronary heart disease (CHD) among RA patients compared to the general population. The second is the rapidly growing body of evidence indicating that chronic systemic inflammation (such as that which occurs in RA) plays an important role of chronic inflammation in CHD. We propose 3 specific aims to investigate this subject: First, we will use a cohort study to test the hypothesis that the incidence of acute MI (the central manifestation of CHD) is higher in RA subjects compared to controls. Second, we will identify high-risk RA subgroups and, using a novel adaptation of the case-cohort design, investigate interactions between RA and the major CHD risk factors (e.g. smoking, **hyperlipidemia,** exogenous estrogens). Third, we will conduct studies on archived autopsy heart tissue to test the hypothesis that coronary atherosclerosis is more extensive in RA subjects compared to matched controls. A unique set of circumstances allows us to address each of these aims rigorously and efficiently. We will incorporate and extend our already assembled population-based RA incidence cohort and identify validated definite acute MI outcomes using the cardiovascular surveillance techniques developed through out NIH-funded companion study, "Coronary Disease Morbidity and Mortality in a Population" (HL59205). Our population-based data resources, with essentially complete enumeration of a geographically defined population, allowed us to design an analytic plan which nearly quadruples the statistical power of our risk factor analyses, compared with typical cohort analyses. Third, the availability of extensive autopsy material (the autopsy rate in this community is four-fold higher than the national rate and all autopsies have been performed at the same center since 1930) provides us with a unique opportunity to assess the pathologic characteristics of atherosclerosis among RA subjects compared to controls. When combined with our experienced multidisciplinary investigative team, these resources lend us a capability, not available elsewhere, to rigorously examine the risks and determinants of coronary heart disease in patients with RA. These results will lay the foundation for a program of research aimed at elucidating the mechanisms for CHD in RA patients and at improving our understanding of the role of inflammation in the pathogenesis of CHD in the general population.

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- **Project Title: HEAT SHOCK IN VASCULAR SMOOTH MUSCLE CELLS**

  Principal Investigator & Institution: Baas, Arnold S.; Medicine; University of Washington Grant & Contract Services Seattle, Wa 98105

Timing: Fiscal Year 2002; Project Start 10-APR-1999; Project End 31-MAR-2004

Summary: (Adapted from applicant's abstract) The goals of the proposal research project are: 1) to prepare and train the candidate for a career in cardiovascular research providing him with the necessary education, environment, and support, and 2) to gain further insight into the role of heat shock proteins (Hsp) in modulating the response of vascular smooth muscle cells (VSMC) to oxidative stress. The candidate will be provided with extensive education in biochemistry, physiology, pharmacology, pathology, signal transduction, research methods, statistics, and epidemiology as it pertains to the cardiovascular system. The candidate will be supported and mentored by this sponsor, Bradford C. Berk who with the research advisory committee will monitor the candidate's progress. Finally, the Department of Medicine and the Division of Cardiology at the University of Washington will provide full commitment and support to developing the candidate's career into an independent investigator. The below proposed project is the first attempt at attaining these goals. Hsps are a family of cellular proteins that are proposed to maintain cell survival. Initially, Hsps were demonstrated to play an important role in protein folding and chaperoning. Recent evidence, however, indicates that Hsps also function to mediate signal transduction and to prevent apoptosis. Hsps are induced by sublethal cellular stress such as hypoxia, ionizing radiation, toxins, cytokines, and reactive oxygen (ROS) such as H2O2, O2-, and OH. ROS are normal products of respiration and metabolism of fatty acids in the presence of O2. However, the generation of excessive quantities of ROS or the failure to scavenge ROS leads to oxidative stress. Risk factors for atherosclerosis such as **hyperlipidemia,** diabetes mellitus, cigarette smoking, hypertension, and hyperhomocysteinemia cause oxidative stress and have been demonstrated to change vessel redox state. The investigators have previously demonstrated that ROS stimulate cultured VSMC proliferation and active intracellular kinase associated with cell growth such as mitogen-activated protein kinases (MAPK). Furthermore, they have demonstrated the novel finding that oxidative stress-stimulated VSMC synthesize and secrete proteins into the extracellular media which in turn activate MAPK in an autocrine and paracrine fashion. Additional characterization of these oxidative stress-synthesized and -secreted proteins resulted in identification of members of the heat shock protein (Hsp) 90 family. In response to oxidative stress, VSMC specifically increase de novo production of intracellular Hsp90 B and stimulate extracellular secretion of pre-formed Hsp90 a. To further characterize the oxidative stress-mediated induction and secretion of Hsp90 in VSMC, they propose the following three specific aims: 1) Determine the role of Hsp90 as mediator of VSMC cytoprotection and anti-apoptosis in response to ROS. 2) Determine the role of heat shock factor (HSF-1) protein phosphorylation by specific MAPK family members in regulation of ROS-stimulated Hsp90 B synthesis in VSMC. 3) Determine the cellular mechanisms responsible for oxidative stress-mediated Hsp90 alpha secretion in VSMC. Elucidating the regulation of the Hsp90 by ROS will provide insights into pathways by which VSMC respond to vessel oxidation-a key process in atherogenesis.

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- **Project Title: HEAVY METALS, OBESITY AND CARDIOVASCULAR RISK**

  Principal Investigator & Institution: Guallar, Eliseo; Epidemiology; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-AUG-2006

  Summary: (provided by applicant): Heavy metals are a heterogeneous group of highly reactive substances, which may act as essential cofactors for physiologic processes and/or as toxic elements. Chromium, in particular, has been associated with obesity,

diabetes, and weight loss. Other heavy metals have been associated with some of the consequences of obesity, including hypertension, **hyperlipidemia,** and cardiovascular disease. The Look AHEAD Study, a large randomized controlled trial of intensive lifestyle intervention for weight loss in obese patients with Type 2 diabetes mellitus, provides an excellent opportunity to address the impact of chromium on weight loss and diabetes control, as well as to assess the impact of other heavy metals on the physiologic consequences of weight loss. We propose an ancillary prospective observational study within the Look AHEAD trial to collect toenail clippings from all participants (n = 5,000) at baseline and at the 1-year visit, and to analyze a random subset of the toenails (1,150 baseline toenails and 480 1-year visit toenails) for their heavy metal content using instrumental neutron activation analysis. Toenails provide a time-integrated measure of heavy metal exposure, while instrumental neutron activation analysis provides the concentrations of about 50 heavy metals in the toenail samples, including chromium. This information will allow us to evaluate the relationship of baseline toenail chromium concentrations to weight loss, as well as the interaction between heavy metals and the beneficial effects of weight loss. The proposed study may provide, valuable insight into the determinants of the efficacy of weight loss interventions. In fact, the Look AHEAD trial, because of its size, may be one of the few studies in which these relationships can be measured reliably. In addition, the ancillary study will permit the setup of a specimen bank of toenails to be used in future case-cohort or nested case-control studies of the association of heavy metals with Look AHEAD endpoints, especially myocardial infarction and cardiovascular death.

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- **Project Title: HIGH FAT FEEDING AND INTRAMYOCELLULAR LIPID ABNORMALITY**

  Principal Investigator & Institution: Guo, Zengkui; Mayo Clinic Coll of Medicine, Rochester 200 1St St Sw Rochester, Mn 55905

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 31-JUL-2006

  Summary: It is now known that intramyocellular triglycerides (imcTG) content in skeletal muscle of obese adults is increased and this abnormality is associated with impaired glucose metabolism in the muscle. However, the pathways responsible for the increase and the link between the increased imcTG and insulin resistance have not been studied in detail. The objective of this application is to determine the factors and pathways that are responsible for the imcTG accumulation, and to determine whether the oxidation of imcTG fatty acids is also increased and, if so, whether it directly affects glucose metabolism. It is hypothesized that elevated plasma insulin and fatty acid levels, as commonly seen in human obesity, independently stimulate imcTG synthesis and synthesis is the primary pathway leading to the increased imcTG accumulation; and that a larger imcTG pool leads to accelerated imcTG oxidation thereby interfering with muscle glucose metabolism. To test the hypotheses, three specific aims will be pursued to answer following questions: 1) Is insulin an anabolic hormone stimulating imcTG synthesis? 2) Does elevated plasma fatty acid concentration increase imcTG synthesis by providing abundant precursors? 3) Is a larger imcTG pool associated with accelerated oxidation of imcTG fatty acids, and if so, how this affects muscle glucose metabolism? A new one-pool model will be applied to determine the rates of imcTG synthesis, turnover and oxidation directly (muscle biopsy) at controlled insulin and fatty acid levels in rats made obese by high fat feeding. The oxidation of imcTG fatty acids and muscle glucose uptake, glycolysis and glycogen synthesis will be determined using multiple tracers to determine the effect of imcTG oxidation on glucose metabolism. Stable isotopic tracers

(13C) and mass spectrometry (GC/MS and isotope ratio MS) will be used to quantitate the kinetics. These studies are designed to answer the questions whether an enlarged imcTG is a chemical entity that imposes a negative effect on glucose metabolism, and whether plasma insulin and fatty acids are responsible for the increased imcTG, and if so, how. Thus, the proposed research will improve the understanding of the mechanism of insulin resistance and imcTG abnormalities in the obese rat that will benefit investigation of human obesity.

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- **Project Title: HIV-ASSOCIATED METABOLIC SYNDROME: ETIOLOGY/TREATMENT**

  Principal Investigator & Institution: Gavrila, Alina N.; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

  Timing: Fiscal Year 2004; Project Start 01-FEB-2004; Project End 31-JAN-2007

  Summary: (provided by applicant): The etiology and optimal treatment options of the HIV-associated metabolic syndrome, characterized by body fat redistribution, **hyperlipidemia,** and insulin resistance have not yet been fully elucidated. However, the mere presence of these metabolic abnormalities suggests increased risk for developing atherosclerotic cardiovascular disease, particularly given the prolonged survival due to HAART regimens. This research proposal includes two complementary studies (an observational study and a clinical trial) focusing on the HIV metabolic syndrome. The overall objective of the observational study is to identify whether serum resistin levels are an independent predictor for the development of insulin resistance, **hyperlipidemia,** and fat redistribution in HIV-infected subjects treated with antiretroviral agents and whether resistin interacts with other hormonal predictors such as leptin and adiponectin. This study consists of two parts: a cross-sectional sub-study aiming at determining associations of resistin levels with metabolic abnormalities, and a longitudinal sub-study assessing the role of baseline resistin levels in predicting development and progression of constituents of the HIV metabolic syndrome after a one-year interval. The interventional study is a 2x2 factorial, randomized, double blind, placebo-controlled clinical trial designed to identify whether fenofibrate arid/or pioglitazone administration improves **hyperlipidemia,** insulin resistance, glycemic control, lipodystrophic changes, and atherosclerosis associated with antiretroviral use in HIV-infected patients.

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

- **Project Title: HUMAN HEME OXYGENASE-1 GENE REGULATION BY OXIDIZED LDL**

  Principal Investigator & Institution: Agarwal, Anupam; Associate Professor; Medicine; University of Florida Gainesville, Fl 32611

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

  Summary: (provided by applicant): Induction of heme oxygenase-1 (HO-l) is an adaptive and cytoprotective response in cells and tissues exposed to oxidative stress of a diverse nature. Recent studies have demonstrated the importance of HO-l expression in atherogenesis. Oxidized LDL (oxLDL) is implicated in the pathogenesis of atherosclerosis, a major cause of morbidity and mortality, specifically in patients with predisposing factors such as diabetes mellitus, hypertension, **hyperlipidemia,** renal disease, and obesity. Our previous studies have demonstrated that exposure of human aortic endothelial cells to oxLDL results in the induction of HO-l. OxLDL is a complex

structure consisting of several chemically distinct components. Our preliminary studies have identified linoleyl hydroperoxide (13-HPODE, LAox), an oxidized C: 18 containing fatty acid, as the major component of oxLDL responsible for HO- 1 induction. Most importantly, such induction occurs via increased HO-l gene transcription through molecular mechanisms different from known inducers of the gene. The studies in this proposal will evaluate the biological role of HO-l induction in response to oxLDL both in vitro and in vivo using HO-l knock out mice as well as delineate the regulatory elements that control oxLDL- mediated HO-1 gene expression in human aortic endothelial cells. Aim IA will evaluate the effects of an atherogenic diet in HO-l deficient mice in vivo. Aim IB will involve in vitro experiments in a model of oxLDL-induced injury in endothelial cells derived from the HO-l deficient mice. Aim IIA will evaluate specific regions of oxLDL-inducible altered chromatin structure of the human HO-l gene. Aim IIB will involve studies to characterize the oxLDL-responsive element using luciferase and human growth hormone reporter genes. The studies outlined in Aim IIIA will evaluate DNA-protein interactions at the single nucleotide resolution by in vivo footprinting and Aim IIIB will evaluate the functional significance of potential DNA-protein binding regions by site-directed mutagenesis. These studies have a potential application for the development of novel molecular approaches to manipulate expression of the human HO-l gene and thus exploit its cytoprotective effects in atherosclerotic cardiovascular diseases, wherein oxLDL is an important mediator.

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- **Project Title: HYPERTENSION / ATHEROSCLEROSIS PARADIGMS**

  Principal Investigator & Institution: Herrera, Victoria Lm.; Associate Professor; Medicine; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 02118

  Timing: Fiscal Year 2002; Project Start 15-AUG-1999; Project End 31-JUL-2004

  Summary: Clinical and experimental data demonstrate unequivocally that hypertension accelerates atherosclerosis. This is an intriguing pathogenic phenomenon since the interaction is quite unambiguous for two complex diseases marked by clinical and genetic heterogeneity. Currently, the mechanisms underlying this interaction have not been elucidated. Strategic animal models are needed to mechanistically dissect pathogenesis. We have developed a transgenic hyperlipidemia- genetic hypertensive rat model by hepatic over-expression of human cholesteryl ester transfer protein (hCETP) in Dahl salt-sensitive (S) rats. Transgene high copy number in Tg[hCETP]53 Dahl S rats elicits aortic, coronary and intramyocardial atherosclerotic lesions and decreased life spans compared with no lesions in non-transgenic Dahl S controls and minor medial changes in Tg[hCETP]25 Dahl S rats with transgene moderate copy number. In this research proposal, we will investigate whether synergistic decrease of NO activity induced by both hypertension and atherosclerosis results in enhanced activated endothelial molecular and cellular changes which are then differentially amplified. as enhanced pro-inflammatory and pro-thrombotic changes leading to progressive vascular disease. The following specific aims will be studied: 1) Determined whether the endothelium of hypertensive, markedly hyperlipidemic Tg[hCETP]53 Dahl S rats exhibit exaggerated endothelial cell activation (marked by enhanced and/or sustained up-regulation of ICAM-1 and P-selectin gene expression and increased monocyte adhesion compared with control age-matched normotensive, markedly hyperlipidemic Tg[hCETP]53 Dahl salt-resistant (R) male rats, and control non-transgenic age-matched hypertensive, normolipidemic Dahl S rats. 2) Determine whether exaggerated activation results in amplified dysregulation through enhanced pro-inflammatory response (marked by increased TNF-alpha expression and increased NF-kappaB activation in

endothelial cells, macrophages) and/or pro-thrombotic response (marked by tissue factor TF expression in endothelial cells, macrophages, intimal smooth muscle cells)--distinct from corresponding arteries in control normotensive, markedly hyperlipidemic Tg[hCETP]53 Dahl R rats as well as in control hypertensive, normo-lipidemic Dahl S rats. 3) Define the hierarchical relationship of hypertension **hyperlipidemia** and decreased NO activity on the acceleration of atherosclerosis by determining which manipulation, high salt diet, Western Type Diet, or NO-inhibitor L-NA treatment will cause Tg[hCETP]25 Dahl S rats to exhibit similar atherosclerotic lesion phenotype similar to Tg[hCETP]53 Dahl S rats. 4) Define the mechanistic role of endothelial NO pathway in the interaction of hypertension and atherosclerosis; sufficient versus essential but not sufficient versus modifying but not essential by early, mid-point, and late-onset L-arginine treatment of Tg[hCETP]53 Dahl S rats and determine whether the acceleration of atherosclerosis by hypertension is differentially attenuated, if not significantly resolved. This research proposal will provide key information on mechanisms that underlie the acceleration of atherosclerosis by hypertension which will identify new strategies for intervention.

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- **Project Title: IMPACT OF SLEEP ON FEEDING AND THE METABOLIC SYNDROME**

  Principal Investigator & Institution: Bass, Joseph T.; Evanston Northwestern Healthcare Evanston, Il 60201

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

  Summary: (provided by applicant): Over the past two decades, an increased prevalence of sleep deprivation in the US has become a major public health challenge. Sleep deprivation been implicated in the epidemic of the metabolic syndrome, a condition characterized by insulin resistance, **hyperlipidemia,** cardiovascular disease and hypertension. Presently, 30% of the US population is overweight or obese and diabetes affects nearly 17% of persons over the age of 65. Recent clinical research indicates that sleep deprivation may pose a risk for the development of diabetes and the metabolic syndrome, however the underlying physiological and pathophysiological basis for the connection between sleep and metabolic homeostasis remains incompletely understood. This application proposes to exploit a novel experimental model of acute and chronic partial sleep deprivation in order to dissect the link between sleep loss and the metabolic syndrome. Already, we have found that chronic partial sleep loss in our animal model reproduces features of the metabolic syndrome including changes in hypothalamo-adrenal axis, decreased leptin and increased fatty acids. We have also made exciting discovery that suggest a role for alterations in the biological clock and clock regulated metabolic pathways that may lead to the metabolic syndrome. We now propose to apply the model we have developed together with molecular genetic tools to investigate the basic mechanisms that link sleep, circadian rhythms, food intake and energy homeostasis. Insight gained from these studies will provide new strategies to prevent metabolic complications associated with sleep deprivation and uncover novel metabolic targets for treatment of obesity and its co-morbidities.

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

- **Project Title: IMPROVING MEDICATION ADHERENCE IN COMORBID CONDITIONS**

  Principal Investigator & Institution: Dunbar-Jacob, Jacqueline M.; Professor; Health and Community Services; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 29-SEP-2000; Project End 31-AUG-2005

  Summary: (investigator's abstract): Improving Medication Adherence in Comorbid Conditions: Approximately 50 percent of persons on prescribed pharmacological therapy have difficulty adhering to their regimen. This difficulty contributes significantly to such adverse outcomes as hospitalization, the development of complications, disease progression, premature disability or death. The costs of poor adherence have been estimated to approach $100 billion dollars a year. Little effort, however, has been directed to the evaluation of adherence intervention strategies and few of those to remedial efforts. A population at particular risk for poor adherence and resulting untoward outcomes are those persons with co-morbid chronic conditions. No efforts have been directed to the remediation of pharmacological adherence problems in this group. It is the aim of this proposed study to evaluate an intervention developed within a problem-solving framework, which has been shown to be effective for a single pharmacological regimen for a single chronic disorder, within a sample on multiple pharmacological therapies for co-morbid conditions. The model for co-morbidity with multiple therapies that we have chosen is Type 2 diabetes with concurrent hypertension and **hyperlipidemia.** This is a prevalent co-morbid condition with high risk for multiple adverse clinical outcomes. Using a randomized, controlled design, we propose to examine the impact of a telephone delivered counseling intervention among 198 poor adherers who are being treated with oral medications for each of these disorders. Subjects receiving adherence counseling will be further randomized into a maintenance arm and an observation arm for an additional six months. All subjects will have adherence and clinical outcomes assessed at baseline (t1), the end of the 6-month intervention (t2), and again after the six-month follow-up period (t3). Potential predictors of adherence and responsiveness to intervention will be examined, including such factors as cognitive and physical function, quality of life, social support, and perceived problem solving ability, and sociodemographic as well as psychosocial factors. Secondarily, we propose to explore the cost-effectiveness of improving adherence with this intervention. A sample of approximately 198 good adherers, identified during screening, will also be invited to continue adherence monitoring for a 12 month period of time to identify the stability of good adherence levels as well as to identify factors that influence that stability.

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- **Project Title: IS THERE A LINK BETWEEN ALZHEIMER'S AND ATHEROSCLEROSIS**

  Principal Investigator & Institution: Grammas, Paula; Shideler Professor; Pathology; University of Oklahoma Hlth Sciences Ctr Health Sciences Center Oklahoma City, Ok 73126

  Timing: Fiscal Year 2004; Project Start 15-JAN-2004; Project End 31-DEC-2007

  Summary: (provided by applicant): Alzheimer's disease (AD) is a neurodegenerative disease that affects over 4 million Americans. We are the first to demonstrate that brain blood vessels release neurotoxic proteins in Alzheimer's disease. However, the factors that cause this vessel dysfunction are not known. It is our hypothesis that risk factors

involved in the pathogenesis of atherosclerosis are also causally linked to the development of vascular-mediated neuronal cell death in Alzheimer's disease. Our studies are timely and important as increasing evidence points to a link between atherosclerosis and Alzheimer's disease. Aim 1: To determine the effects of systemic oxidant stress or **hyperlipidemia** on vascular thrombin release, vascular-mediated neurotoxicity and on the cognitive performance of apoE transgenic mice. Brain blood vessels isolated from apoE knockout or transgenic mice expressing human E3 or E4 are used to assess the role of apoE isoforms on vascular expression of thrombin. Diet-induced hyperhomocystinemia and **hyperlipidemia,** are used to assess the role of oxidant stress and lipids, respectively, on vascular thrombin release and vascular-mediated neurotoxicity. Also, these transgenic mice are utilized to evaluate possible apoE isoform-specific effects of oxidant and lipid stress on impairments in learning and memory. Aim 2: To determine if risk factors involved in the pathogenesis of atherosclerosis are also causally linked to the development of vascular-mediated neuronal cell death in Alzheimer's disease. Brain microvessels are isolated from AD patients and non-demented patients and analyzed for levels and/or activity of thrombin and other possible neurotoxic proteins, including, matrix metalloproteinases (MMPs), inflammatory cytokines and chemokines, and endothelin-l. Protein levels are determined by ELISA and Western blots and Mrna levels assessed by Northern blots and RT-PCR. The role that apoE isoforms play in regulating these proteins is determined by comparing microvessels isolated from patients with different APOE genotypes. In vitro addition of oxygen species or lipid molecules to isolated brain microvessels is used to assess the effects of oxidative stress and lipids, respectively, on release of thrombin, MMPs, inflammatory proteins, and endothelin-l. Apoptosis and necrosis are measured in cultured neuronal cells exposed to these proteins. These results would, for the first time, identify a mechanistic cascade linking cardiovascular risk factors to vascular-mediated neuronal cell death in Alzheimer's disease and identify novel targets for therapeutic intervention.

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- **Project Title: LIPID REGULATION OF VASCULAR AND BONE OSTEOCLASTOGENESIS**

  Principal Investigator & Institution: Demer, Linda L.; Professor; Medicine; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-AUG-2005

  Summary: (provided by applicant): Vascular calcification is now recognized as a widespread, clinically significant process similar to bone formation. Paradoxically, it correlates with osteoporosis. Both are linked to atherosclerosis and **hyperlipidemia.** We have recently provided evidence that oxidized lipids regulate mineralization, promoting matrix calcification by vascular cells and blocking matrix calcification by bone cells in vitro. We further showed that **hyperlipidemia** is associated with significantly reduced bone mineral density and content in mice. Bone mineral density in vivo is regulated not only by osteoblastic activity, but also by resorptive activity of osteoclasts. and effects of oxidized lipids and hyperlipidernia on osteoclastic differentiation and function are not known. In osteoporosis, osteoclastic activity overtakes osteoblastic activity. We now hypothesize that oxidized lipids regulate differentiation and function of mineral-resorbing osteoclastic cells in bone and artery wall. These regulatory effects of lipids on osteoclastic differentiation could also be dependent on factors produced by stromal cells in the two tissues. Specifically, we hypothesize (1) that osteoclast-like cells are present in artery wall as well as in bone and are regulated by oxidized lipids in both tissues, (2)

that oxidized lipids regulate stromal cell production of and response to osteoclastogenic factors such as M-CSF, RANKL, PTH, and IL-6, and (3) that the atheroprotective enzyme paraoxonase also prevents both hyperlipidemia-induced vascular calcification and bone loss in vivo. To test these specific hypotheses we will: 1) examine human and mouse arterial specimens for osteoclastic markers and activity and test whether oxidized lipids affect osteoclastogenesis using in vitro models of vascular and bone tissue, 2) assess stromal cell production of M-CSF, IL-6 and RANKL before and after treatment with oxidized lipids and test stromal cell responsiveness to osteolytic stimuli, PTH and IL-6 in vitro and in vivo. and 3) determine whether deactivation of oxidized lipids by paraoxonase blocks oxidized lipid and hyperlipidemla- induced vascular calcification and bone loss in vitro and in vivo. Elucidating the mechanism by which oxidized lipids regulate mineral resorption will allow novel treatment approaches for osteoporosis and vascular calcification, including the possibility of biologically controlled regression of vascular calcification.

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- **Project Title: LIPOPROTEIN PATHOPHYSIOLOGY**

  Principal Investigator & Institution: Albers, John J.; Research Professor of Medicine; Medicine; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2002; Project Start 01-MAY-1983; Project End 31-MAR-2004

  Summary: Premature vascular disease in young hyperlipidemic subjects remains a major unsolved health problem in terms of pathogenesis and treatment. Recent research advances have led to new markers for genetic analysis, new methods for studying lipoprotein metabolism and atherosclerotic disease progression and regression, and reference values for diagnosing **hyperlipidemia.** With these advances, the opportunity now exists for further in-depth focused studies of lipoprotein physiology and pathophysiology in genetically characterized patients with the objectives of understanding disease mechanisms, developing better treatments, and identifying and preventing early vascular disease. This will be accomplished by focusing our attention on the molecular, genetic and pathophysiological basis of the inherited dyslipoproteinemias associated with premature coronary artery disease with particular reference to familial combined **hyperlipidemia,** familial moderate hypercholesterolemia, familial elevation of Lp(a) and the carrier state for homocysteinemia. Coordinated studies of characterization of the pathophysiological state, the identification of possible molecular biological defects and the evaluation of these results in families by statistical genetic techniques will be performed in each disorder. The role of protein mediated intravascular modification of lipoproteins and the role of oxidation of lipoproteins in each disorder will lead to characterization of these genetic lipoprotein abnormalities. The Program Project, comprised of four coordinated projects, four supporting core facilities and a multidisciplinary team of investigators will combine the expertise in physiology, molecular biology, biochemistry, genetics, immunochemistry, nutrition, endocrinology, metabolism, epidemiology, and statistical genetics, to study lipoprotein physiology and pathophysiology at several levels of biological organization from basic molecular and cell biology through in vivo studies in humans to studies in populations.

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- **Project Title: LIVER TRIGLYCERIDE METABOLISM IN NASH**

  Principal Investigator & Institution: Parks, Elizabeth J.; Food Science and Nutrition; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 31-JUL-2004

Summary: (adapted from the application) Non-alcoholic steatohepatitis (NASH) is a disease of emerging clinical significance. The risk factors for NASH include female gender, non-insulin dependent diabetes, obesity and **hyperlipidemia.** In NASH, the fat that accumulates in the liver is primarily triglyceride (TG) and three sources potentially contribute to this lipid are fatty acids (FA) derived from the diet, those originating in the adipose tissue (FFA in the plasma), and FA newly synthesized in the liver via process called de novo lipogenesis. The origin of the fat that accumulates in the liver has not been extensively investigated previously due to the technical challenges of studying de novo lipogenesis and the limitations of using radioactive isotopes in humans. Recent advances in gas chromatography/mass spectrometry and stable (non-radioactive) isotope methodology now make it possible to study hepatic TG metabolism in vivo. The hypothesis to be tested is that de novo lipogenesis contributes substantially to hepatic TG found in NASH. Further, it is hypothesized that plasma-derived FFA will contribute quantitatively less to the fat stored in hepatocytes and more to the TG that is exported from the liver in lipoproteins. Patients with persistently elevated liver enzymes of uncertain etiology, who are being considered for liver biopsy, will undergo a 5-day, stable-isotope infusion of labeled FA and precursors of FA, preceding the scheduled biopsy. Liver biopsy tissue (100 mg) will be analyzed to determine its biochemical content (TG, cholesterol, phospholipid and FFA), the composition of FA within these fractions, and the enrichment of labeled FA in the tissue (the sources of these FA). Control subjects will be aged- and sex-matched individuals undergoing surgical treatment for obesity who will have an identical isotope infusion before surgery. These methods will be used to accomplish the specific aims: (1) to quantify the concentration of the various lipids in NASH liver samples and samples from obese control subjects; (2) to determine the sources of FA used for lipid synthesis, and the turnover of these lipids in NASH patients and controls; and (3) to determine whether there is a difference between NASH patients and controls with respect to the composition of FA within liver tissue. Liver samples will be graded histologically and the stage of NASH documented semi-quantitatively. Computer tomography will be used to quantify liver size and abdominal visceral fat; ultrasound will also be performed. The results of all of these measurements will be analyzed to determine their relationship with hepatic lipid content. NASH will become more clinically important in the future as the incidence of obesity and diabetes continue to rise in the United States. In combination with the clinical data obtained, an understanding of the contributions of FA sources to liver TG will aid in the development of future treatment strategies for this disease.

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- **Project Title: MAGNETIC RESONANCE OF CARDIAC C13 FLUX & METABOLIC RATE**

  Principal Investigator & Institution: Lewandowski, E Douglas.; Professor; Physiology and Biophysics; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2003; Project Start 01-AUG-1993; Project End 31-JUL-2008

  Summary: (provided by applicant): This proposal exploits the opportunity for a comprehensive 13C NMR evaluation of fatty acid handling within the intact, functioning heart. The overall goal is to further develop and apply our kinetic 13C NMR methods to study the reciprocal relationship between the activity of the key regulator of fatty acid oxidation, carnitine palmitoyl transferase I (CPTI) and turnover of the myocardial triglyceride pool in normal and diabetic animal models. New and exciting findings from the previously funded period enable 13C NMR to distinguish between

oxidative rates in the mitochondria and the rate of long chain fatty acid transport, via CPT1, as well as detect the incorporation rate of 13C-enriched palmitate into the myocardial triglyceride pool, all in the intact, beating heart. Therefore, this study explores the hypotheses that: 1) changes in the regulation of long chain fatty acid oxidation, via CPT1 activity, mediate the turnover rate of myocardial triglycerides and can be evaluated in whole hearts by a comprehensive examination of 13C enrichment kinetics; 2) Alterations in triglyceride content and turnover in the diabetic myocardium occur due to a combination of **hyperlipidemia** and changes in the expression of genes encoding enzymes for fatty acid uptake and oxidation pathways and that these can be distinguished via 13C NMR as independent mediators in the pathogenesis of diabetic cardiomyopathy. This hypothesis will be tested in both in both rat and mouse models of normal, diabetic, and genetically altered cardiac phenotypes. Specific aims are: 1) Determine reciprocal effects of fatty acid oxidation rates on triglyceride turnover via cardiac 13C NMR during partial inhibition of CPT1; 2) Examine long chain fatty acid oxidation rates, CPT1 activity, and triglyceride pool turnover in the hearts of rats with type-I (insulin deficient) diabetes and test for a potential link between triglyceride accumulation and turnover and the activation of protein kinase C; 3) Investigate effects of triglyceride pool size on the reciprocal nature of CPT1 activity and triglyceride turnover in a transgenic mouse model, overexpressing peroxisome proliferator-activated receptor alpha (PPAR-alpha), that mimics the diabetic phenotype for fatty acid and glucose metabolism and allows for dietary control of myocardial triglyceride pool size; 4) Examine long chain fatty acid oxidation rates, CPT1 activity, and triglyceride turnover in a more clinically relevant animal model of type II (insulin resistant) diabetes, the db/db mouse model, versus non-diabetic, wild-type mice.

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- **Project Title: MECHANISM OF PI-RELATED DYSLIPIDEMIA AND ATHEROSCLEROSIS**

  Principal Investigator & Institution: Rader, Daniel J.; Director, Preventive Cardiology; Medicine; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2002; Project Start 15-SEP-2000; Project End 31-AUG-2005

  Summary: (Adapted from the applicant's abstract) Atherosclerotic cardiovascular disease (ASCVD) is becoming an important cause of morbidity and mortality in HIV-infected persons. **Hyperlipidemia** is common in HIV-infected persons and protease inhibitors frequently cause or exacerbate **hyperlipidemia.** Furthermore, it is possible that protease inhibitors may directly promote atherogenesis. Therefore, an understanding of the mechanisms by which protease inhibitors cause **hyperlipidemia** and whether they directly promote atherogenesis is of great clinical importance. The goals of this proposal are: 1) to determine the physiologic mechanisms by which protease inhibitors therapy causes dyslipidemia in humans using lipoprotein kinetic studies with endogenous labeling of apolipoprotein B with stable isotopes; 2) to determine the molecular mechanisms by which protease inhibitors cause dyslipidemia and may promote atherosclerosis by utilizing "humanized" mouse models of lipoprotein metabolism and atherosclerosis. Specific Aim 1: To test the hypotheses that dyslipidemia associated with protease inhibitor therapy is caused by 1) reduced conversion of VLDL to LDL due to reduced triglyceride lipolysis caused early in susceptible patients by protease inhibitors themselves; 2) increased VLDL apoB production associated subsequently with the development of visceral fat accumulation. Specifically, the investigator will perform lipoprotein kinetic studies using endogenous labeling with stable isotopes in two types of studies in human subjects. Studies will use endogenous

labeling with a primed constant infusion of D3- leucine. A compartmental model of apoB-containing lipoprotein metabolism will be constructed and the effect of protease inhibitors on apoB kinetic parameters will be determined. Two types of studies will be performed: a cross-sectional study in HIV patients on PI therapy with lipodystrophy (LD), patients on PI therapy without LD, and patients not on PI therapy without LD as well as control subjects: and a longitudinal study in PI-naive patients who initiate therapy and are studied prior to and twice after initiating therapy. These studies will be performed collaboratively with the other projects in this proposal. Specific Aim 2: To use "humanized" mouse models of lipoprotein metabolism and atherosclerosis to determine the molecular mechanisms by which protease inhibitors cause **hyperlipidemia** and promote atherosclerosis. Specifically, the investigator will use human apoB transgenic mice and administer protease inhibitors to determine effects on lipoprotein kinetics, lipolytic enzymes and expression of specific lipid-metabolism related genes in liver and adipose to determine those that have been up or down-regulated as a result of protease inhibitor therapy. In order to determine whether protease inhibitors promote atherosclerosis, the investigator will administer protease inhibitors to mice prone to atherosclerosis and determine effects on initiation and progression of atherosclerosis. Finally, the investigator will perform micro array analysis of RNA isolated from the aortic arch (a site that reproducibly develops atherosclerosis) to determine the specific vascular genes that have been up or down-regulated as a result of protease inhibitor therapy. These studies will provide novel insights into the mechanisms of PI-associated dyslipidemia and atherosclerosis.

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- **Project Title: MECHANISMS AND STRATEGIES FOR INSULIN RESISTANCE IN AIDS**

  Principal Investigator & Institution: Grinspoon, Steven K.; Associate Professor of Medicine; Massachusetts General Hospital 55 Fruit St Boston, Ma 02114

  Timing: Fiscal Year 2002; Project Start 15-SEP-2000; Project End 31-AUG-2005

  Summary: (Adapted from the applicant's abstract) The lipodystrophy syndrome is a newly recognized syndrome among HIV-infected men and women. The investigator has shown in a recent collaboration with the Framingham Heart Study that patients with lipodystrophy demonstrate a significant insulin resistance syndrome , characterized by hyperinsulinemia, dyslipidemia and increased diastolic blood pressure. Insulin resistance associated with the HIV lipodystrophy syndrome poses a considerable risk for long-term increased cardiovascular disease, but little is known of its mechanism nor has treatment been established. Fat redistribution is strikingly abnormal in affected female patients, but the gender-specific cardiovascular consequences of the insulin resistant phenotype are not known. In this grant proposal this project will determine the gender-specific characteristics of the insulin resistant phenotype in HIV-infected men and women. The investigator will test the hypothesis that truncal fat gain and subcutaneous fat loss contribute independently to the insulin resistant phenotype, and furthermore, that hyperinsulinemia impairs fibrinolysis and disrupts endothelial function leading to increased carotid intimal medial thickness and stenosis. The investigator will test the hypothesis that increased circulating free fatty acids (FFA) resulting from fat redistribution contribute to insulin resistance and increased endogenous hepatic glucose production. Simultaneously, a novel approach to the treatment of insulin resistance in patients with the lipodystrophy syndrome, in which there was shown an effect of metformin to lower insulin levels in preliminary studies. In the final aim of the proposal, the project will investigate in vitro, the independent and

combined effects of PI's and nucleoside analogues on human subcutaneous and visceral adipocytes. These studies will allow us to determine for the first time the depot-specific mechanisms by which these agents may lead to subcutaneous fat loss and visceral fat gain and thereby promote insulin resistance. This project will study the effects of these agent on adipogensis, differentiation, insulin sensitivity and expression of PPAR and other adipocyte regulatory genes using thiazolidinediones to determine whether PPAR gamma activation can rescue the differentiated phenotype. The novel studies in this grant proposal will provide important new information on mechanisms, cardiovascular effects and optimal treatments for insulin resistance in the HIV-lipodystrophy syndrome. The proposed studies represent a significant collaborative effort between clinical researchers, adipocyte biologists, epidemiologists and nutritional biochemists in satisfaction of the mandate of the RFA.

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- **Project Title: MECHANISMS BY WHICH GDM LEADS TO DIABETES IN OFFSPRING**

  Principal Investigator & Institution: Simmons, Rebecca A.; Associate Professor; Pediatrics; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-JUL-2006

  Summary: (provided by applicant) In the human, diabetic pregnancy induces marked abnormalities in glucose homeostasis and insulin secretion in the fetus that results in aberrant fetal growth. Studies have suggested that there are long-term consequences for the offspring of diabetic mothers. We have developed a model of gestational diabetes (GDM) in the rat to determine whether an altered metabolic intrauterine milieu is directly linked to the development of diabetes later in life. Uteroplacental insufficiency is induced in the pregnant rat on day 19 of gestation. Offspring are growth retarded at birth, however they catch-up by 5- 7 weeks of age. At 8 weeks of age they are bred to normal males. During pregnancy these animals develop hyperglycemia, hyperinsulinemia, and **hyperlipidemia** accompanied by impaired glucose tolerance and insulin resistance. Offspring, (F2's) are heavier at birth and remain heavy throughout life. F2's are insulin resistant very early in life and glucose homeostasis is progressively impaired. F2 rats go on to develop diabetes as adults. Although F2 animals display marked insulin resistance, the failure of the Beta-cell to compensate for defects in insulin action is the essential factor coincident with onset of diabetes. This failure of the Beta-cell to compensate may be due to a lack of compensatory increase in insulin secretion, an increased rate of cell death, a reduction in the rate of Beta-cell proliferation, or a combination of these events. The mechanism(s) underlying this lack of Beta-cell compensation and eventual decrease in Beta-cell mass in F2 animals are the focus of this proposal. We hypothesize that mitochondrial DNA damage from hyperglycemia via the production of reactive oxygen species (ROS) results in further escalation of genetic damage in the mitochondria, specifically in mutations. A self- reinforcing cycle of progressive deterioration in mitochondrial function leads to a corresponding decline in Beta-cell function. Finally, a threshold in mitochondrial dysfunction and ROS production is reached and Beta-cell death occurs. The onset of diabetes ensues when a critical level of abnormal Beta-cell insulin secretion combined with Beta-cell loss is reached. We will test the hypothesis that GDM does in fact cause mitochondrial dysfunction, oxidative stress, and deletions in mtDNA in the Beta-cell of the offspring, and whether these effects act synergistically to lead to the development of the Beta-cell failure and type II diabetes. To link the damage to the mitochondria caused by hyperglycemia to the Beta-cell phenotype observed in type II diabetes we will induce

Beta-cell failure in vitro by transferring damaged mitochondria from F2 animals into Beta-cells from unaffected. non-F2 animals.

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- **Project Title: MECHANISMS OF BETA CELL COMPENSATION AND FAILURE**

  Principal Investigator & Institution: Leahy, Jack L.; Professor-Chief, Division of Endocrinolo; Medicine; University of Vermont & St Agric College 340 Waterman Building Burlington, Vt 05405

  Timing: Fiscal Year 2004; Project Start 01-AUG-2004; Project End 31-MAY-2008

  Summary: (provided by applicant): A key pathogenic feature of type 2 diabetes is loss of the a-cell compensation to the insulin resistance that occurs in this disease. The biochemical and molecular nature of this a-cell failure are poorly known, in part because of lack of animal models that faithfully reproduce the natural history of the human disease. This proposal makes use of a newly developed rat model, the 60% pancreatectomy Zucker rat that incorporates the characteristic features of human adipogenic diabetes - obesity, insulin resistance, and **hyperlipidemia.** They are characterized by a 3-week period of relative normoglycemia after the partial pancreatectomy (compensation phase) that is followed by the onset of a-cell dysfunction and mild hyperglycemia (decompensation phase). We will use this model to test the hypothesis of this application that enhanced then impaired a-cell anaplerosis and lipid partitioning are the mechanistic basis for the a-cell compensation and subsequent a-cell failure in these rats. A notable aspect of this application is it stems as a joint effort from the laboratories of Drs. Jack Leahy (Burlington, VT) and Marc Prentki (Montreal, Canada) who have complimentary research expertise in the fields of a-cell anaplerosis/lipid partitioning and the a-cell failure in rodent models of type 2 diabetes. Aim 1 will determine the cellular mechanisms and signaling pathways for theft-cell compensatory growth or loss of a-cell mass in the 60% Px ZF rat model at different stages during the progression to diabetes. Aim 2 will test the hypothesis that the mechanism of a-cell decompensation in the 60% Px ZF rat model is related to failure of compensatory enhanced anaplerosis and lipid signaling processes. Aim 3 will test the hypothesis that the a-cell failure in 60% Px ZF rats is in part due to inadequate proinsulin synthesis relative to secretion. These studies will provide a better understanding of the molecular basis for a-cell compensation and failure, and they hold considerable promise to provide targets for novel pharmaceutical approaches to the prevention or more effective treatment of type 2 diabetes.

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- **Project Title: MENTORED PATIENT-ORIENTED RESEARCH CAREER DEVELOPMENT AW**

  Principal Investigator & Institution: Stein, James H.; Associate Professor; Medicine; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 31-JUL-2006

  Summary: PROPOSAL: (Adapted from the applicant's abstract): Dr. Stein will develop a career in patient-oriented research by obtaining advanced training in clinical research design, biostatistics, lipoprotein biochemistry, and advanced ultrasound research techniques. He also will receive training in the ethical conduct of human subjects research. His long-term goal is to become a nationally and internationally recognized clinical investigator who develops therapeutic strategies and tests for the diagnosis and management of patients with or at risk for atherosclerotic vascular disease. As part of

his research career development plan, Dr. Stein will complete the UWMS Clinical Investigator Preparatory Pathway (CIPP). As part of this program, he will obtain advanced training in research design, biostatistics, and epidemiology through courses and directed study in the UWMS Biostatistics and Medical Informatics Statistical Data Analysis Center. He will obtain training in lipoprotein biochemistry and lipid laboratory techniques through courses and directed study in the UWMS Hospital Lipid and Lipoprotein Laboratory. He will obtain training in advanced carotid ultrasound research techniques in the Center for Medical Ultrasound at Wake Forest University (WFU). Additional instruction regarding ethics and human subjects research regulations, leadership, teaching, and scientific writing are components of the career development plan. The research plan will determine whether the metabolic changes associated with use of human immunodeficiency virus (HIV) protease inhibitors are atherogenic, as determined by their effects on endothelial function (measured by flow-mediated vasodilation of the brachial artery) and early atherosclerosis (measured by carotid intimal-medial thickening). Abnormalities of these parameters, which are obtained by vascular ultrasound techniques, predict adverse cardiovascular events. Dr. Stein also will assess the effects of HIV protease inhibitors on atherogenic lipoproteins using the advanced lipid laboratory skills he obtains in the career development plan. Finally, Dr. Stein will determine if these medications impair postprandial clearance of triglyceride-containing lipoproteins by assessing lipid and lipoprotein responses to an oral fat load.

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- **Project Title: METABOLIC CONSEQUENCES OF ANTIRETROVIRAL THERAPY**

  Principal Investigator & Institution: Weigle, David S.; Associate Professor of Medicine; Medicine; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2002; Project Start 15-JAN-1999; Project End 31-DEC-2003

  Summary: (Adapted from applicant's abstract) A new and poorly understood syndrome that may include central body fat redistribution, **hyperlipidemia,** and hyperglycemia has recently been recognized in individuals receiving highly active antiretroviral therapy (HAART) for HIV infection. It is likely that these metabolic changes, which resemble those seen in Cushing's syndrome, will significantly increase the risk for premature coronary artery disease in treated individuals. Although overt Cushing's syndrome has been excluded in affected individuals, there have been no reported studies based on actual measurement of cortisol production rates or tissue sensitivity to glucocorticoids in subjects receiving HAART. Similarly, it is not known whether HAART regimens may directly stimulate growth of abdominal adipocytes through an effect on PPAR gamma, a key transcriptional activator of preadipocyte differentiation. In this study, 180 HIV-infected individuals about to begin protease inhibitor therapy and 50 uninfected control subjects will be followed for one year with sensitive measurements of regional body composition, lipid and glucose metabolism, cortisol production, and adipocyte gene expression. The Specific Aims of this study are twofold: First, a case definition of the metabolic syndrome will be formulated based on identification of predisposing clinical factors and a comparison of changes in body composition, lipoprotein levels, ans glucose metabolism occurring in subjects over the course of the study. The atherogenicity of the **hyperlipidemia** associated with HAART will be fully defined by a detailed analysis of lipoprotein subfractions. The second aim of the study will be to test the hypotheses that (a) physiological hypercortisolemia + increased cortisol receptor expression, or (b) increased expression or activation of PPAR gamma is abdominal preadipocytes predict the subsequent development of metabolic abnormalities in subjects receiving HAART. The decision of investigate these two

hypotheses was based on both the biological plausibility of the underlying mechanisms and the availability of drugs that might be used to specifically block glucococorticoid action (RU-486) or increase the activation of PPAR gamma in peripheral relative to abdominal preadipocytes (thiazolidenediones). Future trials of these medications, along with a great deal more basic research, are clearly justified by the increasing and sustained use of HAART to deal with the worldwide epidemic of HIV infection.

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- **Project Title: METABOLIC CONSEQUENCES OF HAART: CYP3A AND P-GP**

  Principal Investigator & Institution: Greenblatt, David J.; Professor and Chair; Pharmacol & Exper Therapeutics; Tufts University Boston Boston, Ma 02111

  Timing: Fiscal Year 2002; Project Start 15-JUN-2001; Project End 31-MAY-2004

  Summary: The human immunodeficiency viral protease inhibitors (HIV PIs), as a component of multiple drug therapy with other Highly Active Anti- Retroviral Therapies (HAART), have profoundly changed the prognosis and quality of life for individuals with HIV infection. Nonetheless PIs and other HAART drugs are not curative of HIV, and resurgence of viral load (possibly with resistant forms) from viral reservoirs ("breakthrough") remains a clinical problem of ongoing concern. Pharmacokinetic variability - - particularly that leading to periods of low or undetectable levels of one or more HAART drugs - - may predispose to breakthrough and resistance. One major source of variability derives from the relation of the kinetics of HAART drugs to the human Cytochrome P450-3A (CYP3A) isoforms, which mediate the metabolism of the HAART drugs themselves and many other compounds, and to P-glycoprotein (P-gp), a transport protein localized in GI tract mucosa and the blood-brain barrier. Many of the important HAART drugs are inhibitors and/or inducers of CYP3A and/or of P-gp, producing complex and time-dependent interactions involving their own metabolism (i.e.,autoinduction) as well as interactions with other coadministered classes of medications. Dysregulation of CYP3A by HIV PIs, and possibly other HAART components, has been linked to metabolic consequences of HIV such as lipodystrophy, insulin resistance, and **hyperlipidemia.** The present proposal utilizes related clinical and molecular techniques to provide definitive data on the extent, time course, and consequences of the interaction of HAART components with CYP3A and P-gp, using the PI ritonavir as the index compound. A. In clinical studies, midazolam (given I.V. and orally) is used as a probe CYP3A substrate to determine the effects of ritonavir on hepatic and gastrointestinal CYP3A function under the following conditions: control, prior to ritonavir exposure; with acute ritonavir exposure (inhibition); during extended ritonavir exposure (combined induction and inhibition); following extended ritonavir exposure (induction only). Parallel studies of P-gp regulation are performed using fexofenadine as the index substrate. B. A human adenocarcinoma cell culture model will evaluate the time-course and concentration-dependence of P-gp upregulation by HAART drugs, based on immunoquantitative techniques as well as functional assays of P-gp dependent cell exclusion of a fluorescent probe. This multidisciplinary proposal provides a clinical and scientific basis to assess the effects of currently available as well as experimental HAART medications on human CYP3A and P-gp.

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- **Project Title: MINERALIZATION STUDIES RELATED TO ATHEROSCLEROSIS**

  Principal Investigator & Institution: Hsu, Howard Ht.; Pathology and Lab Medicine; University of Kansas Medical Center Msn 1039 Kansas City, Ks 66160

Timing: Fiscal Year 2002; Project Start 10-APR-2002; Project End 31-MAR-2005

Summary: Atherosclerotic calcification has profound effects on arterial wall rigidity and is closely associated with morbidity and mortality. However, the mechanisms of dystrophic calcification remain poorly understood. A recent in vitro study demonstrated that vesicles isolated from atherosclerotic human and rabbit aortas can initiate calcification. It remains to be established: 1) whether **hyperlipidemia,** which causes atherosclerotis, can promote calcification through the production or activation of calcifiable vesicles and 2) how vesicle-mediated calcification is regulated through an active process. To address these issues, the present proposal will focus on the following Specific Aims: 1) To support the role of vesicles in calcification by evaluating the hypothesis that calcifiability of vesicles precedes and progressively increases with aortic calcification during atherogenesis. At different periods of time, aortic vesicles will be isolated from the control and experimental animals and compared for their calcifiability. Fourier transform spectroscopy will be used to characterize the types and to measure the amount of mineral deposited in aorta and by isolated vesicles. A similarity in the amounts and types of mineral deposited by vesicles and in aortas would strongly implicate vesicles in atherosclerotic calcification. 2) To test the hypothesis that vesicle-mediated calcification is closely regulated by cellular, matrix, and vesicle constituents. Cholesterol and its derivatives hydroxycholesterol and deoxycholate detergent known to stimulate cell- and vesicle- mediated calcification will be used to study the mechanisms whereby **hyperlipidemia** can lead to calcification. The effects of macrophage products such as osteopontin on vesicle calcification and tumor necrosis factor (TNF-alpha) on pathogenesis of calcifying vesicles will be investigated for a better understanding of the active process involved in vesicle-mediated calcification. A long-term goal of the project is to identify factors that initiate and control dystrophic calcification, thereby contributing to the knowledge that may lead to the prevention and treatment of atherosclerotic calcification.

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- **Project Title: MINORITY PREDOCTORAL FELLOWSHIP PROGRAM**

  Principal Investigator & Institution: Estrada Smith, Daria; Anatomy and Cell Biology; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

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

  Summary: (provided by applicant): Obesity, insulin resistance, atherosclerosis and **hyperlipidemia** are interrelated traits that have a significant impact upon morbidity and mortality. To better understand the relationship between these traits and the genes, which underlie them, we are developing a mouse model that utilizes the synteny between mouse chromosomes 2 to human chromosomes 20. Here three congenic mouse strains were created each of which contains 30 cM of DNA from chromosome 2 from the obesity resistant, insulin resistant CAST strain introgressed onto the background of an insulin resistant, obesity susceptible BL6 strain. Comparing the congenic mouse strains to the parental BL6 strain permits us to ask questions regarding the genes, which underlie the relevant traits. More importantly this comparison will allow us to investigate the interacting pathways involved. Specifically, this project aims to characterize the metabolic impact that each CAST locus has upon the BL6 background by identifying variations in body mass, fat distribution, bone density, insulin sensitivity and production, atherosclerosis and lipid profiles. Diets that enhance one or more of these traits will also be used to further assess the metabolic effect of each CAST locus. Concurrently global comparisons of gene expression using microarray analysis from

adipose, muscle, pancreas and liver tissues will be performed to assess the contributions that specific genes within each congenic region make to the metabolic variations identified above. Relevant pathways will be identified utilizing the commercially available software (GeneSpring) designed to correlate gene expression profiles with pathways cited in the literature (KEGG).

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

- **Project Title: MOLECULAR GENETIC APPROCHES IN ATHEROSCLEROSIS RESEARCH**

  Principal Investigator & Institution: Lusis, Aldons J.; Professor; Molecular Biology Institute; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2002; Project Start 01-JUL-1984; Project End 31-DEC-2005

  Summary: The theme of this proposal is the examination of altered states of triglyceride metabolism contributing to coronary artery disease. The program addresses this theme using the mouse and human homology at the pathological, physiological, biochemical, genomic and molecular levels. Of the 5 projects in this proposal, Projects 3 will mostly involve studies in mice while 2 projects principally involve studies in humans, with 5 cores providing phenotyping, genotyping, sequencing, positional cloning, biostatistical and administrative support. Our major approach will be use genetic defects in mice and humans to identify underlying genes that contribute to altered states of triglyceride metabolism. We will emphasize familial combined **hyperlipidemia** (FCHL), a genetically complex disease characterized by increased plasma triglyceride metabolism. We will emphasize familial combined **hyperlipidemia** (FCHL), a genetically complex disease characterized by increased plasma triglyceride and/or cholesterol levels which accounts for up to 20% of premature coronary artery disease. Dr. Lusis' project will extend previous genetic studies in mice to systematically delineate genetic factors contributing to triglyceride metabolisms. Notably, will combine forces with Dr. Peltonen's Project to identify the gene affected by Hyplip1, a mutation in the mouse that causes combined **hyperlipidemia** and co- localizes with a homologous FCHL locus in humans. Dr. Wong's Project will focus on the structure-function properties of lipoprotein lipase (LPL), an enzyme central to triglyceride metabolism, as well as identifying genetic loci that affect LPL expression and may contribute to the LPL deficiency observed in FCHL. Dr. Reve's Project will isolate the genes, and characterize the function of the corresponding gene products, for two mouse mutations affecting triglyceride metabolism, fatty liver dystrophy (fld) and combined lipase deficiency (cld); these mutations are characterized by insulin resistance (fld) and LPL deficiency (cld) that often associated with FCHL. Dr. Rotter's project will use a combination of genome wide linkage and candidate gene association approaches to characterize genetic risk factors for coronary artery disease in human populations by identifying genes for lipid and lipoprotein variation in FCHL. Dr. Peltonen's project, using the power of a discrete population isolate (the Finn's) will perform fine mapping of a recently identified FCHL locus to isolate the predisposing FCHL gene by a positional cloning approach. Importantly, the Finnish FCHL locus is syntenic with mouse Hyplip1, and Project V will assist in isolating the mouse gene to complement and aid in the identification of the homologous human FCHL gene. Thus, the 5 projects provide a coordinated approach to identifying major genes affecting triglyceride metabolism and predisposing to coronary artery disease.

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- **Project Title: MURINE MODELS OF NON-ALCOHOLIC STEATOHEPATITIS**

  Principal Investigator & Institution: Igolnikov, Alexander C.; Medicine; Northwestern University Office of Sponsored Research Chicago, Il 60611

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

  Summary: (provided by applicant): Non-alcoholic fatty liver disease (NAFLD) is the most common cause of abnormal liver function tests in the United States. NAFLD represents a spectrum of disease including hepatic steatosis, steatohepatitis (NASH) and steatohepatitis with fibrosis or cirrhosis. Although NASH has been associated with obesity, diabetes, **hyperlipidemia** and insulin-resistance, in fact, little is known about the pathophysiology of NASH, and the molecular and cellular mechanisms responsible for the development of NASH remain virtually unexplored. The administration of a methionine- and - choline deficient (MCD) diet to mice serves as an animal model of NASH. In this proposal, we will employ the MCD model and wild-type and mutant mice to: 1) investigate the role of hepatic Phospatidylethenolamine-N-Methyltransferase (PEMT) and S-adenosylmethionine (AdoMet) in the pathophysiology of NASH; 2) to determine the import of hepatic phospatidylcholine (PC) secretion in the development of NASH; and 3) and further define the role of endotoxin in the pathophysiology of NASH. The studies will help elucidate the pathophysiology, and thus better allow for rational new therapeutic approaches, for this common hepatic disease.

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

- **Project Title: NATURAL HISTORY OF MENOPAUSE IN HIV INFECTED DRUG USERS**

  Principal Investigator & Institution: Schoenbaum, Ellie E.; Professor; Montefiore Medical Center (Bronx, Ny) Bronx, Ny 104672490

  Timing: Fiscal Year 2002; Project Start 20-SEP-2000; Project End 31-AUG-2005

  Summary: Description (from applicant's abstract): This proposal seeks to investigate the process of menopause among HIV-infected women. The specific aims are to describe: 1) the impact of HIV infection and drug use on menopausal symptoms and biologic markers; 2) attitudes and knowledge about menopause among HIV infected and drug using women, 3) the impact of H IV infection and drug use on bone mineral density before and after menopause: and 4) impact of HIV infection and antiretroviral therapy (HAART) on dyslipidemia, insulin resistance, and development of post-menopausal cardiovascular disease. The proposal is for a five-year prospective study of 750 middle-aged women in the Bronx, half of whom are HIV infected, and half at risk for HIV infection. A significant number of the participants will come from existing cohorts HIV Epidemiologic Research Study (HERS) which is ending and HIV Epidemiologic Research on Outcomes Study (HEROS) which will continue until 2002. Women will be recruited from the community to complete the newly proposed cohort.

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- **Project Title: NITRIC OXIDE-SUPEROXIDE IN LIPID INDUCED VASCULAR DISEAS**

  Principal Investigator & Institution: Katusic, Zvonimir S.; Professor; Mayo Clinic Coll of Medicine, Rochester 200 1St St Sw Rochester, Mn 55905

  Timing: Fiscal Year 2002; Project Start 05-FEB-1998; Project End 31-JAN-2006

  Summary: (provided by applicant): Abnormal endothelium dependent vasorelaxation due to reduced nitric oxide bioavailability in the blood vessel wall is a key component of

vascular disease associated with **hyperlipidemia,** hypertension, diabetes mellitus, obesity and atherosclerosis and may be important in the pathogenesis of atherosclerosis. While there are many potential causes of decreased NO bioavailability in the blood vessel wall, decreased NO generation or increased NO degradation via interaction with superoxide anions may play a pivotal role. Gene therapy approaches to atherosclerosis may include systemic delivery of genes to the liver to treat risk factors or local delivery to the vessel wall to enhance NO bioavailability to augment blood flow, enhance new vessel formation or limit cell proliferation in the vessel wall. A gene therapy approach utilizing local delivery of NOS gene to the vessel wall has advantages as nitric oxide has pleiotropic anti-atherogenic effects in the vasculature. In addition, a better understanding of the role of superoxide in endothelial dysftinction in various stages of atherosclerosis may allow the therapeutic effects of superoxide dismutase overexpression to be explored. In this proposal we will test the following hypotheses a) individual NOS isoform may have distinct characteristics for altering vascular reactivity in the normal and diseased blood vessel wall, b) adeno-associated virus vectors can be used to transfer the NOS gene to the vascular wall resulting in long term alteration of vascular reactivity without inflammation and c) long term overexpression of NOS in the blood vessel wall of the hypercholesterolemic rabbit will improve endothelium dependent vasorelaxation and delay the progression of atherosclerosis and d) increased scavenging of superoxide via SOD gene transfer may increase NO bioavailability and reverse lipid-induced endothelial dysfunction. These experiments will determine which NOS isoform is best at altering vascular function, examine the functional effect of prolonged expression of eNOS in the rabbit carotid artery using AAV vectors, examine the effect of NOS overexpression on progression of atherosclerosis and elucidate the role of superoxide in the pathogenesis of endothelial dysfunction in various stages of atherosclerosis.

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

- **Project Title: NUTRITION INTERVENTION: METABOLIC COMPLICATIONS OF HIV+**

  Principal Investigator & Institution: Woods, Margo N.; Associate Professor; Family Medicine & Cmty Health; Tufts University Boston Boston, Ma 02111

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-JUL-2007

  Summary: (provided by applicant): As the HIV population survives and ages, a new syndrome is being observed that appears to be affected by PI medications but is also seen independent of PI use. This syndrome is characterized by **hyperlipidemia,** lipodystrophy and insulin resistance. Elevated triglycerides are a common observation with or without hypercholesterolemia. Since statin do not reduce serum triglycerides and may be counter-indicated to lower serum cholesterol because of potential liver damage in the HIV+ population that are on PI, dietary interventions have been getting more attention. Literature suggests that a diet lower in fat with reduced levels of saturated fat relative to polyunsaturated fat, increased omega 3-fatty acids intake, high fiber, and use of carbohydrates lower in glycemic index may be beneficial when they were studied individually. We propose to use a nutrition intervention in a HIV+ population that has elevated triglycerides (>220 mg/dl) to test whether a diet that combines all of these factors can have a significant effect on reducing serum triglycerides. The nutrition intervention will be a low fat diet (25% of calories from fat) with a 1:1:1 ratio of Saturated:Monounsat: Polyunsaturated fat, high in fiber (40 g/day) with carbohydrates of lower glycemic index (< 70 whenever possible). This diet will contain 3 g/day of omega 3-fatty acids which will be supplemented with 3.0 g of omega

3-fatty acids from capsules to give a total of 6 g/day of omega 3-fatty acids and a ratio of n-6/n-3 of 4:1. In addition to measuring triglycerides, serum cholesterol and its sub-fractions will be determined as well as insulin area under the curve (AUC) and body composition using CT scan. HIV+ participants eligible for the study (N=100) would be randomized into a control or nutrition intervention group and be tested for changes after 3 weeks, 13 weeks and 6 months of intervention. During the first 3 weeks the intervention group will be given all their meals at the hospital General Clinical Research Center, followed by an additional 10 weeks in which some food products are supplied to them along with the continued use of omega 3-fatty acids supplements at 3 gms/day (in 10 capsules). After 13 weeks the participants will be asked to continue to take the omega 3-fatty acid capsules but food products high in n-3 fatty acids will not be supplied. A 6-month follow-up will then remeasure all the study parameters to determine if the nutrition intervention group had experienced an improvement of the listed risk factors compared to the control group.

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

- **Project Title: OSTEOGENIC REGULATION OF MACROVASCULAR CALCIFICATION**

  Principal Investigator & Institution: Towler, Dwight A.; Chief, Division of Bone and Mineral Dise; Barnes-Jewish Hospital Ms 90-94-212 St. Louis, Mo 63110

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-JUL-2003

  Summary: (provided by applicant): Epidemiology suggests that diabetes and hypercholesterolemia increase risks for atherosclerotic & osteoporotic diseases. The regulation of vascular calcification is poorly characterized; the LDLR -/- mouse model & human valve specimens implicate heterotopic osteogenic mechanisms. It is important to understand aortic calcification and metabolism in our aging population since pharmacotherapies implemented to promote bone formation & preserve bone mass may alter progression of calcific vasculopathy. The 3 specific aims of this proposal are: Aim 1: "To characterize the activities of prolonged dysmetabolic exposure and osteoanabolic pharmacotherapy on orthotopic (skeletal) vs. heterotopic aortic osteogenic gene expression programs, using the diabetic LDLR -/- mouse as a model." In vivo data suggest overlapping yet distinct transcription mechanisms are rate limiting in the initiation of orthotopic vs. aortic calcium deposition. We will directly assess the aortic vs. osseous responses to osteoanabolic pharmacotherapy in the presence or absence of the dysmetabolic state. PTH will be used as a relevant, prototypic osteoanabolic stimulus in the dysmetabolic LDLR -/- mouse model. Gene expression of key osteogenic transcription factors, morphogens, & matrix molecules will be quantified by fluorescence RT-PCR, & spatially resolved by in situ hybridization. Temporo-spatial deposition of aortic calcium will be quantified by image analysis of von Kossa stained sections. Aim 2: "To identify the transcriptional mechanisms that regulate aortic mesenchymal cell osteogenic gene expression, using the osteopontin (OPN) & Msx2 promoters as models for study." The goal is to identify specific DNA-protein interactions that mediate responses to dysmetabolic signals (e.g., diabetes, hyperlipidemia) that control expression of these key osteogenic genes in vascular smooth muscle cells, peri-aortic adventitial cells, and osteoblasts using (a) transfection and gel shift analyses in primary cell cultures and cell lines; and (b) cDNA cloning techniques. Aim 3: "To identify if the gene expression programs elaborated during aortic calcification in the diabetic, hyperlipidemic LDLR -/- mouse provide a molecular phenocopy of human aortic calcification via molecular analysis of calcified human valves." We will determine if human aortic valve calcification quantified by spiral CT is

associated with up-regulation of specific osteoblast transcriptional regulatory programs controlled by Msx2, Dlx5, & Runx2/Cbfa1/Osf2 (osteoblast transcription factors). Gene expression will be quantified by fluorescence RT-PCR and spatially resolved by in situ hybridization. A sub-aim will validate methods for quantifying aortic valve calcium content by spiral CT for future studies of patients treated with osteoprotective agents.

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- **Project Title: OXIDANTS, EICOSANOIDS, AND ENDOTHELIUM IN DIABETES**

  Principal Investigator & Institution: Cohen, Richard A.; Associate Professor; Boston Medical Center Gambro Bldg, 2Nd Fl, 660 Harrison Ave, Ste a Boston, Ma 02118

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

  Summary: (provided by applicant): Oxidant stress is widely recognized to play a role in functional alterations that develop in cells exposed to hyperglycemia and **hyperlipidemia** in the diabetic milieu, and has been implicated as a mechanism that accelerates atherosclerosis in diabetes. The mechanisms by which diabetes increases oxidant stress, and those by which oxidant stress modifies endothelial function are poorly understood. Our preliminary studies establish new insights into how elevated glucose increases oxidant stress and the mechanisms by which its effects on cell function are mediated. Exposure of cultured human endothelial cells to elevated glucose for 7-10 days increases the production of both NO and superoxide anion (O2-), and consequently decreases the bioactivity of NO as indicated by decreased levels of cyclic GMP. Further evidence that NO is inactivated by reacting with O2- to form the reaction product, peroxynitrite (00N0-) is found in the increased levels of its reaction product with tyrosine, 3-o-nitrotyrosine, found in the cells. While the function of many proteins may be affected, we have found that prostacyclin synthase (PGIS) is particularly susceptible to tyrosine nitration; the levels of nitrated PGIS increase and its activity decreases in endothelial cells grown in elevated glucose. This may not only explain why diabetes decreases levels of PGI2, but also why increases have been noted in its precursor PGH2 that activates thromboxane A2 receptors (TPr). Our studies have shown that activation of TPr can modulate ICAM-1 and VCAM-l expression in human endothelial cells. The expression of adhesion molecules is enhanced by 02-, and indeed, exposure to elevated glucose enhances adhesion molecule expression. Thus, oxidant stress induced by elevated glucose may modulate the activity of PGIS and stimulation of TPr, thereby modulating adhesion molecule expression. Indeed, we have found that blockade of TPr inhibits atherosclerosis in the Apo E deficient mouse, a model in which diabetes enhances atherogenesis. There are three specific aims: 1) to determine the mechanism by which elevated glucose and fatty acids increases production of NO and 02- and causes tyrosine nitration and inactivation of PGI synthase, 2) to determine the role of TPr stimulation by eicosanoid products due to endothelial cell oxidant stress and PGI synthase inactivation in causing the increased leukocyte adhesion and apoptosis caused by high glucose and fatty acids, and 3) to determine if oxidant stress and PGI synthase inactivation contributes to the increased atherogenesis caused by diabetes in transgenic mouse models.

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

- **Project Title: PACIFIC REGION DIABETES EDUCATION PROGRAM**

  Principal Investigator & Institution: Chang, Healani K.; None; University of Hawaii at Manoa Honolulu, Hi 96822

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

Summary: (provided by applicant): The goal of the proposed University of Hawaii at Manoa (UHM) Pacific Region Diabetes Education (Pride) Program is to expose high school and undergraduate students to the exciting discovery of scientific inquiry early in their academic training to increase the likelihood they choose to pursue a biomedical career path. The aim of this proposal is to fill the nation's shortage of minority individuals in biomedical research careers. We plan to achieve this objective by offering the student research assistants a ten-week mentored laboratory experience and a well-structured educational enrichment component. Proposed projects for the student includes the genetics of obesity in Hawaii's multi-ethnic populations, autonomic neuropathy, metabolic disorders and alternative medicine, **hyperlipidemia** and insulin resistance. It is anticipated through the proposed "hands on" laboratory experiences and enrichment activities the students research environment will be enhanced. Educational activities to develop both the students research capabilities and their interests in pursuing a biomedical career includes orientation week, scientific communication skills, verbal skills training, seminar series in responsible conduct of research, time management, and environmental and health safety training. The primary learning environment will be in the laboratory with a seasoned research mentor. Students will also have the opportunity to interact with junior and senior minority undergraduates at UHM's Haumana Biomedical Program MBRS and MARC U'STAR Program. A common objective of these two programs is to increase the number of underrepresented minorities in the biomedical sciences who choose to pursue the PhD degree. These two well established programs offer Pride program students the opportunity to visit off-campus laboratories, as well as on-campus seminars, workshops, and informal discussions with visiting minority scientists. Hawaii's geographically isolated location heightens the value of such research experiences for the Pride students who will be making decisions on post-high school and post-baccalaureate careers

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- **Project Title: PERILIPIIN AND LIPOLYSIS**

  Principal Investigator & Institution: Greenberg, Andrew S.; None; Tufts University Boston Boston, Ma 02111

  Timing: Fiscal Year 2004; Project Start 15-JAN-1999; Project End 31-MAR-2008

  Summary: (provided by applicant): Adipocyte lipolysis contributes significantly to the pathogenesis of obesity-associated diseases by increasing levels of circulating free fatty acids (FFA). FFA promote insulin resistance and type 2 diabetes. My laboratory's long-term goal is to elucidate molecular mechanisms of lipolysis regulation. The proposed studies will investigate structure / function relationships of Perilipin A (Peri A), a lipid droplet- associated phosphoprotein that regulates lipolysis mediated by hormone sensitive lipase (HSL) and non-HSL lipase(s). Peri A acts dually as a suppressor of basal lipolysis (in the absence of hormonal stimulation) and as a potent enhancer of protein kinase A (PKA)-stimulated lipolysis (in the presence of hormonal stimulation). Despite its important regulatory role, the primary sequences and the mechanism(s) by which Peri A regulates lipase actions have not been determined. Our preliminary studies indicate that Perilipin regulates lipolysis via multiple regulatory domains, which exhibit surprising lipase specificity. The proposed studies will 1) identify the minimal domains of Peri A that modulate basal and PKA-stimulated lipolysis by HSL and non-HSL lipase(s), 2) determine the relative role of PKA phosphorylation sites in PKA- stimulated lipolysis by HSL and non-HSL lipase, and 3) define the in vivo effects of altered Peri A expression, Peri A truncations and Peri A PKA site mutants using Peri A transgenic and Peri null mice. Our adipocyte and systemic studies will measure basal lipolysis, lipolytic

response to beta-adrenergic agents, and antilipolytic response to insulin. These studies will provide in vivo proof of concept tests of how Peri A expression levels, regulatory domains, and phosphorylation sites regulate basal and stimulated lipolysis. These data will be directed to the prevention and treatment of diabetes, **hyperlipidemia** and other obesity - associated disorders.

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- **Project Title: PERINATAL HYPOXIA: ADRENOCORTICAL-METABOLIC ADAPTATIONS**

  Principal Investigator & Institution: Raff, Hershel; Professor; Medicine; Medical College of Wisconsin Po Box26509 Milwaukee, Wi 532260509

  Timing: Fiscal Year 2003; Project Start 01-JAN-1999; Project End 31-DEC-2006

  Summary: (provided by applicant): Hypoxia during the perinatal period and during early infancy is a significant cause of mortality and morbidity. Adrenocortical hormones are a vital component of the adaptation to hypoxic stress. Furthermore, neonatal hypoxic **hyperlipidemia** is a significant clinical entity, and changes in specific lipid metabolites alter adrenal function. The long-term objective of this proposal is to characterize the short and long-term consequences of perinatal hypoxia on the control of the hypothalamic-pituitary-adrenal (HPA) system and lipid metabolism in the rat. Specific Aims 1 and 2 will evaluate the effect of neonatal hypoxia on the control of the hypothalamic-pituitary-adrenal axis by evaluating intracellular and systemic controllers of steroidogenesis, the timing and mechanisms of the stress-hyporesponsive period (SHRP), and the negative feedback control of CRH and POMC expression and ACTH release. Specific Aim 3 will characterize the long-term sequellae of perinatal hypoxia by evaluating subsequent HPA responses to stimuli in the adult rat. Specific Aim 4 will more fully characterize neonatal hypoxic **hyperlipidemia** by analyzing the interaction of neonatal hypoxia and glucocorticoid therapy, and by performing metabolomic analysis. Neonatal hypoxia from birth is accomplished by exposing newborn rats (with their lactating dams) to a hypoxic environment. Perinatal hypoxia is accomplished by exposing late-gestational pregnant rats to hypoxia and allowing them to deliver in a hypoxic environment. Physiological, biochemical and molecular assessment of adrenocortical function is performed by ACTH injection in vivo, using dispersed cells, evaluating StAR and PBR expression, and measuring CBG and glucocorticoid clearance. Hypothalamic-pituitary function is assessed by measuring stress- and CRH-induced ACTH release, by evaluating feedback sensitivity, and by analyzing pituitary, hypothalamic, and hippocampal function and pertinent receptor/hormone expression. Metabolic function is assessed by analysis of hepatic enzyme activity, as well as complete metabolomic analysis of serum and hepatic lipids. Characterization of the hypothalamic-pituitary-adrenal and metabolic adaptations to perinatal hypoxia can lead to new diagnostic approaches and therapies to minimize morbidity and mortality.

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

- **Project Title: PEROXISMAL AND MITOCHONDRIAL B-OXIDATION IN OBESITY**

  Principal Investigator & Institution: Lee, Wai-Nang P.; Professor; Harbor-Ucla Research & Educ Inst 1124 W Carson St Torrance, Ca 905022052

  Timing: Fiscal Year 2002; Project Start 15-AUG-2000; Project End 31-JUL-2004

  Summary: Peroxisomal and mitochondrial beta-oxidation are two principal pathways of fatty acid oxidation which regulate the nature and concentration of intracellular acyl-CoA and energy rich molecules. The integration of these two systems permits the animal

to adapt to a wide range of nutrient composition without suffering from hyperglycemia or **hyperlipidemia.** This application proposes to investigate the role of these two pathways in the adaptation to nutrient composition and in the development of obesity and diabetes in the Zucker obese and diabetes model. Specific Aim 1: Test the hypothesis that the contribution of peroxisomal and mitochondrial beta-oxidation varies depending on the chain length and desaturation of the fatty acid (nutrient specific). Specific Aim 2: Test the hypothesis that two hormonal systems (insulin and leptin) affect fatty acid synthesis and oxidation differently to regulate gluconeogenesis and lipogenesis. Specific Aim 3: To examine peroxisomal and mitochondrial oxidation in obesity and diabetes using Zucker obese and Zucker diabetic models. Specific Aim 4: To test the hypothesis that the effect of PPAR ligands on fatty acid oxidation interacts with the leptin receptor signaling pathway to improve both glucose and lipid metabolism. A key feature of this proposal is the use of [1-13C]- and [U-13C]-fatty acids and mass spectral technologies to determine the relative contributions to the acetyl-CoA pool from fatty acyl chain shortening and elongation (peroxisomes) to mitochondrial beta-oxidation. These studies should provide new conceptual and experimental tools for the study of fatty acid oxidation regulation, a central issue in the pathophysiology of obesity and Type II diabetes.

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- **Project Title: PLACENTAL VASCULAR COMPROMISE AND PRETERM DELIVERY**

  Principal Investigator & Institution: Thorp, John M.; Professor; Obstetrics and Gynecology; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 01-SEP-2001; Project End 31-AUG-2006

  Summary: (provided by applicant): There is substantial interest in determining the etiology of preterm delivery (PTD). Despite much effort, the cause remains elusive and effective prevention measures do not exist. Uteroplacental vascular compromise (UPVC) via inflammation, thrombosis, or atherosis is a biologically plausible cause of preterm delivery, albeit not adequately explored. We propose to test his hypothesis by conducting a prospective, epidemiologic study of UPVC and by integrating information about known risk factors for PTD. Placental histopathologic examination and morphometric analysis of the basal plate will be done to assess compromise of placental vessels. We will explore novel, possible antecedents of such compromise, dyslipidemia and insulin resistance, using nuclear magnetic resonance analysis of lipid subclasses and fasting insulin-glucose ratios. Given the inaccessibility of the uteroplacental vasculature in ongoing gestations at midpregnancy, we will utilize non-invasive measures of UPVC, Doppler velocimetry of the uterine artery, and maternal serum alpha fetoprotein to indirectly evaluate vascular function. In addition, we will carefully evaluate tobacco and cocaine use, nutrition, and changes in vaginal microflora within our cohort. The data will enable us to thoroughly assess whether UPVC constitutes a distinct etiologic pathway for PTD and help to identify modifiable risk factors. We will utilize cohort and case-cohort techniques, refined in our present research, to answer these questions. Blood, urine and vaginal fluid are collected twice between 15 and 20 weeks and between 24 and 29 weeks gestation. Hair will be collected after delivery. All subjects will complete two telephone interviews and two self administered questionnaires regarding various behaviors, dietary intake, physical activity, and psychosocial stressors. Placentas will be collected at the time of delivery and histopathologic analysis will be completed by an experienced perinatal pathologist for cases and a non-case subgroup. Nuclear

magnetic resonance measurement of lipoprotein subclasses will be done to assess dyslipidemia. Insulin glucose ratios will be measured from fasting blood samples. We expect to enroll a cohort of 1800 women with 250 preterm deliveries and a randomly selected non-case subgroup (n=500). We will analyze the relationship between UPVC and PTD using logistic regression. Given 1) the size of the study, 2) thorough histopathologic assessment of the placenta, 3) extensive questionnaire data, 4) biologic markers of exposure to bacterial vaginosis, insulin resistance, dyslipidemia, and cocaine use, and 5) the careful assessment of potential confounding factors, this study promises to markedly advance our knowledge of the potential role of UPVC in the etiology of PTD.

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- **Project Title: POST-DDP FOLLOW-UP STUDY**

  Principal Investigator & Institution: Kahn, Steven E.; Medicine; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2003; Project Start 20-AUG-1994; Project End 31-JAN-2008

  Summary: (provided by applicant): The Diabetes Prevention Program is a multicenter controlled clinical trial examining the efficacy of an intensive life-style intervention or metformin to prevent or delay the development of diabetes in a population selected to be at high risk due to the presence of impaired glucose tolerance (IGT). Development of diabetes, defined by 1997 ADA criteria, is the primary outcome while cardiovascular disease and its risk factors are important secondary outcomes. The DPP began recruitment in mid-1996. At the time of this application, total study exposure is a mean of approximately 3 years (range 2 to 5) with a total of approximately 10,000 patient years in the 3,234 volunteers in the 3-arm study. On the basis of a statistically significant and clinically compelling decrease in the development of diabetes in the life-style intervention and metformin-treated groups (58% and 31% reductions, respectively) compared with the placebo treated group, the DPP Data Monitoring Board and NIDDK ended the masked treatment phase of the study in May, 2001, one year earlier than originally planned. This application is designed to take further advantage of the scientifically and clinically valuable cohort of DPP volunteers and the large volume of data collected during the study. The highly compliant DPP cohort, including 45% minorities, is the largest IGT population ever studied. Moreover, the subcohort that has developed diabetes (n approximately 700) has been followed from near the exact time of diabetes onset. Clinically important research questions remain in the wake of the DPP. The carefully collected, centrally measured and graded data in this cohort should help to answer, definitively, a number of important questions regarding the clinical course of IGT and early onset type 2 diabetes. Specific aims include: 1. Examine the long-term effects and durability of prior DPP intervention on the major DPP outcomes including diabetes, clinical cardiovascular disease, atherosclerosis, CVD risk factors, quality of life and cost-benefit; 2. Determine the clinical course of new onset type 2 diabetes and IGT, in particular regarding microvascular and neurologic complications; 3. Determine the incidence of cardiovascular disease (CVD), CVD risk factors and atherosclerosis in new onset type 2 diabetes and IGT; and 4. Examine topics 1-3 in minority populations, men vs. women, and in older subjects in the DPP. The current application is for 5 years of funding, although the some of the goals of the projects described will require a 10-year study.

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- **Project Title: POSTPRANDIAL LIPEMIA AND ENDOTHELIAL FUNCTION IN ACCORD**

  Principal Investigator & Institution: Ginsberg, Henry N.; Professor; Medicine; Columbia University Health Sciences Po Box 49 New York, Ny 10032

  Timing: Fiscal Year 2002; Project Start 01-SEP-2001; Project End 31-AUG-2005

  Summary: (provided by applicant): The ACCORD trial will use two connected 2x2 designs to test the efficacy of (a) optimal glucose control (HbA1c = 6.0%) versus standard control (HbA1c + 7.5%) in 10,000 patients with type 2 diabetes mellitus, (b) more intense systolic blood pressure control (120 mm Hg) versus less intense control (140 mm Hg) in 4,200 of those patients, and (c) combined low density lipoprotein cholesterol lowering, triglyceride lowering, and high density lipoprotein cholesterol raising versus only low density lipoprotein cholesterol lowering in 5,800 of those patients. The primary outcome for the overall ACCORD trial is a combination of non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death. The comparison of lipid-altering therapies will be carried out in the Lipid Arm of ACCORD, in which the 5,800 subjects will all be treated with simvastatin and, in addition, be randomly assigned to receive either fenofibrate or placebo. The main ACCORD trial will measure only fasting blood samples for lipids, lipoprotein fractions, and apolipoproteins. In the proposed ancillary study, we will compare the effects of simvastatin plus fenofibrate with the effects of simvastatin alone on postprandial lipemia in 250 ACCORD patients at 4 sites in the Northeast Network. In addition, we will compare the effects of the two treatment strategies on baseline and postprandial endothelial function, and on markers of coagulation, endothelial function, and oxidative stress. The propose ancillary study will provide a unique opportunity to determine possible mechanisms whereby simvastatin plus fenofibrate therapy will be associated with reduced cardiovascular events in the overall ACCORD trail. The study is divided into three specific aims. Specific Aim A: To carry out high fat load studies of postprandial lipemia in patients who are participating in the Lipid Arm of the ACCORD trial and compare postprandial excursions of triglycerides, triglyceride-rich lipoproteins, retinyl palmitate, and remnant lipoprotein cholesterol in patients receiving fenofibrate plus simvastatin with those postprandial excursions in patients receiving only simvastatin. Specific Aim B: To determine brachial artery dilatation in response to increased blood flow post- forearm ischemia just prior to, and five hours after, ingestion of a high fat load in the two patient groups. Specific Aim C: To determine baseline levels of PAI-1, fibrinogen and factor VII, and postprandial excursions of factor VII, sVCAM-1, sICAM-1, and sE-selectin in the two patient groups. ACCORD provides a unique opportunity to compare, in detail, the effects of statin therapy alone with statin plus fibrate therapy on several emerging risk factors for atherosclerotic cardiovascular disease in a representative subgroup of the ACCORD cohort that is being followed for cardiovascular endpoints.

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- **Project Title: PROTEASE INHIBITOR RELATED ADIPOGENESIS IN HIV INFECTION**

  Principal Investigator & Institution: Agrawal, Krishna C.; Regents Professor and Chairperson; Pharmacology; Tulane University of Louisiana New Orleans, La New Orleans, La 70112

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 31-MAY-2004

  Summary: (Provided by applicant) The clinical use of HIV-1 protease inhibitors (PIs) in highly active anti-retroviral therapy (HART) has led to significant improvements in the

prognosis and quality of life in HIV-1 infected patients. However, long-term use of PIs has resulted in side effects such as peripheral lipodystrophy, **hyperlipidemia,** insulin resistance, and disruption of the adipogenic process. Our preliminary studies have shown that PIs suppress adipogenic differentiation in 3T3-L1 cells and the addition of TNFalpha further suppressed the rate of adipogenesis. In contrast, the insulin sensitizing agent, troglitazone, blocked this suppression even in TNFalpha sensitized cells. The primary goal of the proposed research is to investigate the molecular mechanisms involved in the PI-induced modulation of adipogenesis and to test the hypothesis that preadipocytes are sensitized by HIV-1 induced inflammatory cytokine TNFalpha and/or HIV-1 Tat protein, to PI-induced disruption of adipogenesis. This will be achieved by the following specific aims: 1.) To determine the in vitro effects of PIs on adipogenic differentiation in human bone marrow stromal progenitor cells. Transcripts of early, middle and late genetic markers i.e., pref-1, lipoprotein lipase (LPL) and GAPDH, respectively will be determined. Levels of nuclear transcription factors, PPAR-gamma and C/EBP-alpha will be determined by transient transfection assays and gel mobility shift assays. 2.) to determine the sensitizing effect of the HIV-1 induced inflammatory cytokine, TNFalpha and/or HIV-1 Tat protein on PI-induced inhibition of adipogenic differentiation in human bone marrow stromal progenitor cells. 3.) To determine the in vitro effects of PIs on the activity of ECM degrading proteases in human stromal adipogenic progenitor cells. Fibrinolytic activity in undifferentiated and differentiated cells will be monitored by using a chromogenic plasmin substrate. The ECM production at different stages of differentiation will be determined by SDS-PAGE electrophoresis and the activation of ECM degrading proteolytic enzymes (MMPs) will be monitored by gelatin zymography. Real time RT-PCR studies will monitor gene expression of tPA, PAI-1/2 and MMPs/TIMPs which are involved in the fibrinolytic cascade. 4.) To investigate the ameliorative effects of insulin sensitizers on PI-induced lipodystrophy. We will investigate the efficacy of thiazolidinediones (rosiglitazone and pioglitazone) and biguanides (metformin) in suppressing the effects of PI-induced inhibition of adipogenic differentiation. These studies will delineate the molecular mechanisms that may be responsible for the adipogenic side effects induced by the PIs in the presence of HIV infection.

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- **Project Title: PROTEASE INHIBITOR-INDUCED HYPERLIPIDEMIA IN AIDS**

  Principal Investigator & Institution: Brown, Virgil W.; Professor of Medicine; Medicine; Emory University 1784 North Decatur Road Atlanta, Ga 30322

  Timing: Fiscal Year 2002; Project Start 28-SEP-2000; Project End 31-JUL-2005

  Summary: (Adapted from the applicant's abstract) HIV-protease inhibitors (PI) prevent the maturation of nascent virions and are thus very effective in blocking further infection in HIV-positive patients. Significant reductions in mortality from AIDS have been achieved with the use of PI. Cross-sectional studies, however, have suggested accelerated atherosclerosis in HIV-positive patients receiving PI therapy and this may be associated with high prevalence of several risk factors for atherosclerosis: **hyperlipidemia,** hyperglycemia, insulin resistance and fat redistribution. The exact mechanisms underlying these metabolic changes are not known. Based on homology studies, HIV-protease inhibitors may interfere with the function of the low density lipoprotein receptor-related protein (LRP) and the cytoplasmic retinol binding protein (CRBP). LRP is responsible for the hepatic uptake of intestinal lipoproteins transporting dietary fats and fat- soluble vitamins such as vitamin A. Inside the cell, the transport of retinoic acid by CRBP may interact with peroxisome proliferator activator receptor

(PPAR) and thus affect the production of apoC-III and the differ- entiation of adipocytes. Using non-radioactive tracers, we propose to examine the changes in lipoprotein metabolism associated with HIV infection and the therapeutic use of PI. The metabolism of oral retinol will be examined with respect to the effect of PI on LRP. The production of apoC-III, a PPAR- regulated apolipoprotein linked to hypertriglyceridemia and diabetes, will be examined with respect to its association in PI-induced hypertriglyceridemia. While **hyperlipidemia** may be associated with atherosclerosis, it cannot explain the accelerated progression of the disease. Changes in physiological and biochemical responses with oxidative stress associated with postprandial lipemia will be examined as a possible mechanism for accelerated disease progression. A comprehensive longitudinal study with new markers for CAD will also be conducted to characterize the progression of the risk factors with PI. In a subset of patients with **hyperlipidemia,** the efficacy of combined therapy with vitamin A, fibrates, and thiazoladinediones will be evaluated. These are specific agents that are effective in reducing triglyceride as well as improving insulin resistance.

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- **Project Title: QUALITY OF LIFE OUTCOMES >= 5 YRS POST HEART TRANSPLANT**

  Principal Investigator & Institution: Grady, Kathleen L.; Nursing Director; Rush University Medical Center Chicago, Il 60612

  Timing: Fiscal Year 2002; Project Start 01-APR-2000; Project End 31-DEC-2004

  Summary: The purpose of this 5 years prospective, longitudinal study is to identify variables that are associated with and predict six outcomes of adult patients at 5 years to 10 years after heart transplantation (HT). The six outcomes are survival, functional ability, emotional status, work ability, satisfaction with HT, and perceived quality of life. Specific study aims are (1) to determine how variance in demographic, physical, and psychosocial factors over time is concurrently related to variance in the six outcomes over time (2) to identify demographic, physical, and psychosocial predictors of the six outcomes (3) to examine how physical and psychosocial factors that are related to the six outcomes change longitudinally (4) to examine the impact of age, gender, racial / ethnic background, and complications after HT on outcomes over time and (5) to examine the effect of using various statistical methods for handling missing data in order to improve the accuracy of prediction of outcomes. A prospective, longitudinal design will be used. Data will be collected every 6 months beginning at 5 years through 10 years after HT. Inclusion criteria are (1) >= 5 years post HT (2) age >= 21 years (3) able to read and write English, and (4) physically able to participate. Patients will complete a booklet of instruments, and chart data will be gathered. Variables to be measured include demographic variables (ex. age, gender, race, and marital status), physical variables (ex. medical history, medications, exercise testing, and complications), and psychosocial variables (ex. perceived health status, stress, coping, and social support), and the six outcome variables (within a stress, appraisal, and coping model). Statistical analyses will include longitudinal, multi-variable regression methods for repeated measures and parametric modeling of outcomes. Health-Related Implications. These data will provide information regarding (1) long-term benefits versus risks of HT, (2) patients at risk for poor outcomes, (3) and targets for interventions to improve outcomes.

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- **Project Title: RACIAL DISPARITIES IN HEALTH OUTCOMES FOLLOWING CABG**

  Principal Investigator & Institution: Hravnak, Marilyn; Acute/Tertiary Care; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

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

  Summary: (provided by applicant): More than 12 million people in the U.S. have coronary heart disease (CHD), the 2nd leading cause of hospitalization. The CHD death rate is higher for African Americans than for any other racial or ethnic group for which data are recorded. Although coronary artery bypass grafting (CABG) is one of the most common invasive interventions used to treat CHD, African-Americans are less likely to undergo CABG than Caucasians with equivalent severity of disease, and experience higher post-surgical morbidity and mortality. We do not yet have a full understanding of the complex factors that cause these disparities. Some attribute the cause to physiologic or genetic underpinnings, while others contend that race is a social construct with powerful financial consequences impacting health status and health access. Most prior research examining racial disparities in post-CABG outcomes has utilized retrospective analyses, has not controlled well for confounding factors, has limited outcome assessment to morbidity and mortality, and has not accounted for the impact of health-care access upon outcomes. The purpose of the proposed research is to describe differences in CHD-modifiable risk factors, health care access and utilization, and post-surgical outcomes over time in matched African-Americans and Caucasians undergoing isolated CABG, using a prospective between-subjects repeated measures comparative survey design. Subjects will be matched by age, gender, number and source of conduit vessels, and income. Data on modifiable risk factors, health care access and utilization, and outcomes (complications, health-related quality of life and functional status) will be measured at baseline, 3 and 6 months, and compared to determine relationships and effects. My long-term career goal is to develop an independent program of research to reduce health and healthcare disparities in African-Americans undergoing invasive cardiac procedures. To meet this goal, I have developed an intensive training plan to improve my ability to: 1) design and conduct prospective research to understand and reduce disparities in patients with CHD, 2) improve my understanding of issues impacting racial minority health and health-care disparities, and expertise in conducting minority-focused studies, 3) manage and analyze longitudinal data (emphasizing prediction modeling), and 4) prepare and administer grants by participating in multidisciplinary and inter-institutional activities with expert researchers.

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- **Project Title: RAPAMYCIN FOR THE TREATMENT OF RENAL ANGIOMYOLIPOMAS**

  Principal Investigator & Institution: Bissler, John J.; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 452293039

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

  Summary: (provided by applicant): Targeted molecular therapy is the ultimate objective for the management of neoplasia, but only a few examples exist in practice, due in large part to the complexity of genetic events that result in unregulated cell growth. Tuberous sclerosis is an inherited cancer syndrome associated with the formation of hamartomas in multiple organs, including angiomyolipomas in the kidney, caused by well-characterized inactivating mutations at genetic loci that encode the interacting proteins,

tuberin or hamartin. Elegant studies have recently elucidated the pivotal role of the tuberin/hamartin complex in the checkpoint control of the Akt signaling pathway that regulates cell growth and division. Rapamycin, an FDA immunosuppressive approved drug used to prevent renal transplant rejection, mimics the function of the tuberin/hamartin complex by binding to a protein downstream of Akt called mammalian target of rapamycin (mTOR) and inhibiting the phosphorylation of more distal elements that control cell cycle and protein translation. Rapamycin has been shown to specifically inhibit the growth of tuberin and hamartin deficient cells from humans, rodents and flies, and to produce tumor regression in rats and mice. The consensus opinion of the recent Tuberous Sclerosis Complex Research conference in Chantilly, Virginia was that the preclinical evidence for the use of rapamycin in TSC was sufficiently compelling to warrant a human trial. The objective of the current study is to determine if rapamycin reduces the volume of angiomyolipomas. This goal will be accomplished by treatment of thirty patients with angiomyolipomas, either in the setting of tuberous sclerosis, or a related disease associated with mutations in tuberous sclerosis genes called sporadic lymphangioleiomyomatosis, with dose-adjusted rapamycin for a period of one year. The size, number, volume and tissue composition of renal angiomyolipomas will be monitored by MRI scans of the kidney, performed prior to treatment, at two months, four months, and every six months. Other manifestations of TSC, including brain, skin and lung lesions, will also be monitored with appropriate clinical, functional and imaging techniques. The minimal rapamycin dose that produces an effect, defined as a greater than 10% decrease in angiomyolipoma volume, will be titrated beginning with doses that result in subimmunosuppressive serum levels to those that produce levels in the low to modestly immunosuppressive range. Toxicities, as defined by the NCI common toxicities criteria, will be carefully monitored, reported, and expeditiously addressed. Successful completion of the aim of this study will help to establish tuberous sclerosis as a valuable model for targeted molecular therapy for neoplasia.

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- **Project Title: REGULATION OF TROPHOBLAST DIFFERENTIATION AND FUNCTION**

  Principal Investigator & Institution: Sadovsky, Yoel; Associate Professor; Obstetrics and Gynecology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2002; Project Start 22-SEP-2001; Project End 31-JUL-2006

  Summary: (provided by applicant): The focus of our research is placental differentiation and function. These processes are essential for intact embryonic development. We seek to elucidate the impact of the intra-uterine environment on placental function, and consequently fetal growth. An adequate supply of proteins, carbohydrates and fat is obligatory for fetal development Transfer of these nutrients is regulated by a set of well-orchestrated signals, programmed by genetic and environmental cues. Whereas our understanding of placental import of proteins and carbohydrates has markedly advanced in recent years, the mechanisms that govern transport of fatty acids in placental trophoblasts are largely unknown. Recent data implicate the nuclear receptor PPARy in regulation of fatty acid transport. This conclusion is supported by the following observations: (1) PPARy is an essential determinant of adipose tissue differentiation. (2) PPARy regulates the transcription of several genes that encode fatty acid transporters. (3) PPARy -I- embryos exhibit intrauterine growth restriction and subsequently fetal death, associated with diminished size of fat globules within the labyrinthine placenta. In addition, we have recently found that PPARy is expressed in

the human placenta, where it influences trophoblast differentiation in a ligand- specific manner. Correspondingly, human trophoblasts express several fatty acid transporters. We therefore hypothesize that PPARy is a pivotal regulator of fatty acid uptake by placental trophoblast. To test our hypothesis, we address the following questions: Does PPARy regulate the expression of placental fatty acid transporters? Does this regulation translate into a different degree of fatty acid import into trophoblasts? What mechanisms underlie the effect of ligandactivated PPARy on trophoblast differentiation and fatty acid transporter expression? Our studies are likely to unveil previously unrecognized pathways to placental dysfunction and sub-optimal intrauterine growth, which have direct implications for development and behavior in early childhood. Furthermore, fetal growth restriction is associated with metabolic disorders in the adult, including atherosclerosis, hypertension, diabetes and **hyperlipidemia.** Hence, insight into fetal disease may shed light on novel approaches designed to improve adult health.

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- **Project Title: ROLE OF ANGIOTENSIN II IN ATHEROSCLEROSIS**

  Principal Investigator & Institution: Kon, Valentina; Associate Professor; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

  Timing: Fiscal Year 2002; Project Start 01-APR-1992; Project End 31-MAR-2007

  Summary: Description (provided by applicant) Angiotensin II (Ang II) has a critical role in tissue destruction in a variety of chronic conditions. Ang II antagonism has become a dominant therapeutic intervention in a number of cardiovascular, renal and hypertensive disorders that has unexpectedly revealed benefit in atherosclerosis. Atherosclerosis is characterized by some of the same processes that destroy other tissues, however, its pathophysiology is unique in its absolute dependence on lipid deposition within the vessel wall. Thus, although the acute sequelae of atherosclerosis occur later in life, the lipid deposition begins in utero and vascular remodeling proceeds throughout childhood. This underscores that further understanding of atherogenesis can lead to preventive measures that can begin in childhood. The PI's preliminary data suggest that non-hypertensive dose of Ang II promotes initiation of atherosclerotic lesion without affecting the lipid profile. Clinical and animal studies suggest that Ang II affects local vascular accumulation of lipids, although the precise mechanisms are not understood. Monocyte infiltration and uptake of lipid constitute the hallmark of atherosclerosis, namely, formation of macrophage foam cells. Macrophages have recently been revealed to have a crucial role in atherosclerosis. Thus, macrophages can provide sufficient lipid acceptors to correct **hyperlipidemia** and prevent atherosclerosis, conversely, even without affecting the plasma lipid profile, perturbations in macrophage lipid metabolisms, especially lipid efflux, promotes atherosclerosis. How Ang II relates to macrophage function is not well known. The PI's preliminary data indicate that Ang II regulates macrophage accumulation following injury; that macrophages are a source of Ang II; that Ang II promotes development of atherosclerotic lesions; that macrophages in the atherosclerotic lesion express AT1 receptor; and that macrophages deficient in AT1 receptor have more lipid efflux. These observations form the basis for these projects, which is to define the role of Ang II within the vessel walls and within macrophages in atherosclerosis. We will use chimeric mice with transplantation of genetically engineered hematopoetic stem cells into genetically engineered mice. The effects of bone marrow-or vessel-deficiency in Ang II on atherosclerosis will be assessed in vivo. In addition, in vitro macrophage studies will examine the role of Ang II in atherogenic processes including macrophage lipid handling, migration and apoptosis.

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- **Project Title: ROLE OF CHLAMYDIA PNEUMONIAE INFECTION IN ATHEROGENESIS**

  Principal Investigator & Institution: Kuo, Cho-Chou; Professor; Pathobiology; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2002; Project Start 01-APR-1997; Project End 31-MAR-2004

  Summary: (Adapted from the Applicant's Abstract): Chlamydia pneumoniae (TWAR) is a common human respiratory pathogen. In recent years, there has been mounting evidence showing that this organism might play a role in atherosclerosis. Because coronary heart disease is a leading cause of death in this country, the overall goal is to investigate the immunopathogenic mechanisms by which C. pneumoniae infection contributes to the development of vascular disease. The proposed studies will exploit our recent findings from mouse model studies linking C. pneumoniae infection and atherosclerosis and in vitro cell culture studies on C. pneumoniae infection of arterial wall cells. The mouse models that will be used are C57BU6 and strains derived from this background strain including, apoE-deficient and TNF-A receptor and apoE double knockout mice. Atherosclerosis in C57BU6 mice can be induced by feeding with a high fat/high cholesterol diet, while apoE mice develop atherosclerosis spontaneously on a regular diet. The specific aims are to 1) further evaluate the synergistic effect of C. pneumoniae infection and **hyperlipidemia** on atherogenesis by infecting mice with C. pneumoniae followed by feeding animals with a high fat/high cholesterol diet and measuring the atherosclerotic lesion development using computer assisted morphometry; 2) study the effects of C. pneumoniae infection on key components in the inflammatory process of atherosclerosis that promote atherosclerotic lesion development by recruiting lymphocytes/macrophages and eliciting inflammatory responses at lesion sites. In vitro, in vivo, and ex vivo systems will be used to assay the expression of leukocyte adhesion molecules and adherence of macrophages to the endothelial surface. The effect of TNF-A on lesion development will be investigated by infecting TNF-A receptor and apoE double knockout mice and measuring lesion development using computer assisted morphometry; 3) assess the role of macrophages in the establishment of persistent C. pneumoniae infection of atheromatous lesions using cell culture to analyze vascular cell interactions and the effect on infectivity, growth and persistence of C. pneumoniae, and characterize the growth of C. pneumoniae in macrophages loaded with low density lipoproteins (foam cells). The proposed studies should prove invaluable for understanding the disease process and developing better measures for eradication or prevention of C. pneumoniae infection and for reducing atherosclerosis and coronary heart disease.

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- **Project Title: ROLE OF SCAVENGER RECEPTORS IN RENAL FIBROSIS**

  Principal Investigator & Institution: Eddy, Allison A.; Professor; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

  Timing: Fiscal Year 2002; Project Start 01-APR-1992; Project End 31-MAR-2007

  Summary: Description (provided by applicant) Progressive renal disease is caused by a process of fibrosis that relentlessly destroys normal renal architecture and function. The number of patients with end-stage renal disease continues to rise exponentially, at an annual cost to Medicare that now exceeds $12 billion. The goal of the proposed studies is to determine how abnormalities of lipoprotein metabolism, which are frequently present

in patients with renal disease, contribute to the pathogenesis of renal fibrosis. The overall hypothesis to be tested is that macrophage scavenger receptors process low density lipoproteins that have been oxidatively modified within the kidney to initiate fibrosis-promoting events. It is further hypothesized that this pathway worsens fibrosis in the face of hypercholesterolemia. Three Specific Aims are proposed. (1) To determine the effects of hypercholesterolemia on the severity of renal fibrosis and to delineate the pattern of renal scavenger receptor expression in murine models of renal fibrosis. (2) To investigate the role of the macrophage scavenger receptor class A type I/II (SR-AI/II) and scavenger receptor CD36 in renal fibrosis. (3) To elucidate intrarenal changes in pro-oxidant and anti-oxidant enzymes that could promote lipoprotein oxidation in murine models of renal disease associated with **hyperlipidemia.** These in vivo studies will be based on four murine models of renal disease. The functional significance of the two best characterized macrophage scavenger receptors, which are also known to participate in atherogenesis, (SR-AI/II and CD36), will be determined by comparing renal disease severity between wild-type animals and scavenger receptor-deficient animals. Bone marrow transplantation studies will be done to distinguish between the role of renal and macrophage scavenger receptors. Our long-term objective is to provide a scientific basis for the development and use of new therapies for patients with progressive renal disease. It is anticipated that the results of the proposed studies will prove that hypercholesterolemia, intra-renal oxidation of low density lipoproteins and scavenger receptor-dependent interactions with oxLDL represent an important pathogenetic pathway of progressive renal damage.

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- **Project Title: ROLE OF THE LOWER GUT IN THE CONTROL OF ENERGY BALANCE**

  Principal Investigator & Institution: Koopmans, Henry S.; University of Calgary 2500 University Dr Nw Calgary, Ab

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

  Summary: Surgery has been the most successful treatment for morbid obesity. The main objective of this grant proposal is to determine why lower gut signals generated in bypass surgery have been so successful in causing reduced food intake and body weight loss. We recently discovered that lower gut signals also cause a 10-25 percent increase in energy expenditure. One objective of this grant proposal is to determine how stimulation of different lengths of the ileum, caecum and colon affect energy balance and the plasma levels of the lower gut hormones: neurotensin; PYY and GLP1. Another objective is to determine the role of the extrinsic nerves to the ileum in altering food intake, energy expenditure and body weight by doing ileal transplantation surgery or denervation of the superior mesenteric nerves. A time course of the changes in energy expenditure, upper gut tissue growth and plasma lower gut hormone levels resulting from ileal transposition will be investigated in preparation for a later peptide infusion study. The role of the various macronutrients in changing energy balance and lowering body weight will be assessed by feeding various diets to rats with a 20 cm segment of ileum moved up to the mid-duodenum. The short-term objective of this research is to understand the internal control of daily intake and energy expenditure. The long-term objective is to find a medical treatment (drug or hormone analog) for obesity. In Western societies, obesity is a major medical problem that causes a great deal of human suffering. Obesity is associated with such chronic and debilitating conditions as diabetes, cancer (breast, endometrial, prostate and colon), hypertension, **hyperlipidemia,** stroke and

heart disease. An effective medical treatment for obesity would improve the quality of life for millions of people and would reduce the cost of long-term health care.

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- **Project Title: SIGNAL TRANSDUCTION IN ATHEROSCLEROSIS**

  Principal Investigator & Institution: Fitzgerald, Garret A.; Professor; Pharmacology; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2004; Project Start 07-APR-1999; Project End 31-MAR-2009

  Summary: (provided by applicant): This program continues to focus on elucidating the discrete regional susceptibility to atherogenesis. In particular, the complex interplay of mechanical forces and chemical mediators which impinge on platelet vascular interactions and on cells of the vessel wall and their interaction with the extracellular matrix will be elucidated. Distinct and overlapping signaling pathways will be integrated by genomic and proteomic interrogation of determinants of the balance between susceptibility to and protection from atherosclerosis. Particular attention will be paid to how traditional risk factors, including age, **hyperlipidemia** and gender condition cell signaling pathways of relevance to inflammation and oxidant stress. In Project 1 the role of the eicosanoid pathway downstream of the cyclooxygenase enzymes will be examined. Genetic and pharmacological approaches will be combined to elucidate the distinct roles of prostaglandins in the development and regression of atherosclerosis, blood pressure control and the response to thrombosis. Metabolomic analyses and novel quantitative indices of oxidative stress will be utilized to integrate the impact on atherosclerosis in vivo with the response to inflammatory and oxidant stimuli VSMC in vitro, as phenotypic outcomes in vivo are related to genomic and proteomic consequences of receptor deletion in vitro. In Dr. Bennet's project a careful analysis will be performed of the role that transmembrane and cytoplasmic domains play in the regulation of the integrin Alpha-v Beta-3. Particular emphasis will be placed on elucidating the structural constraints that govern formation of homomeric and hetromeric interactions between domains of this integrin, which is of relevance to adhesive interactions between vascular cells. These concepts will also be extended to the platelet collagen receptor, the integrin Alpha-2 Beta-1 where structural information will inform the design of specific small molecule antagonists, tested in the models utilized in Project 1. In Dr. Rader's project, we shall investigate the domains of ApoE that are relevant to upregulation of COX-2 in VSMC and the receptors and signaling pathways relevant to this response. A common approach with Project 1 will be adopted in the genomic and proteomic analysis of the response to ApoE. In Project 4 we shall elucidate the mechanism by which CD44, which we have shown to be of relevance in atherogenesis, impacts on integrin dependent cell spreading and actin polymerization. Particular emphasis will be placed on elucidating how CD44 and its ligand, hyaluronic acid, modulate the cell cycle. Finally, we will utilize mice expressing eGFP fluorescent tagged cyclin A to investigate the role of CD44 deletion on cell proliferation during atherogenesis and in the response to injury in vivo. Finally, in Project 5 we shall examine the effect of gender and **hyperlipidemia** on the discrete expression of genomic subsets in regions of the pig aorta susceptible to and protected from atherogenesis. These studies will be complemented by studies of laminar and disordered laminar shear in vitro: RNA silencing and receptor deletion will be used to elucidate the functional importance of these observations. This program will take an integrated approach to the study of humoral and mechanical signaling in vascular cells. Factors which underlie the cell to cell heterogeneity of this interaction are likely to contribute to the focal nature of atherogenesis.

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- **Project Title: STRUCTURE/FUNCTION ANALYSIS OF THE UROKINASE RECEPTOR**

  Principal Investigator & Institution: Cines, Douglas B.; Professor; Pathology and Lab Medicine; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2002; Project Start 16-AUG-1999; Project End 31-JUL-2004

  Summary: Urokinase (uPA) contributes to physiologic processes (e.g fibrinolysis, angiogenesis and wound healing) and pathophysiologic processes (e.g. inflammation, atherosclerosis and metastasis) by promoting cell adhesion and proteolysis of extracellular barriers. We observed that the complex of single chain uPA (scuPA) and its receptor (uPAR) is enzymatically active, pro-adhesive and relatively resistant to PAI-1. Our data also indicate that multiple sites of interaction between scuPA and uPAR are required for optimal enzymatic and adhesive activity. However, the molecular basis of these interactions and how they are controlled are incompletely understood. We identified a peptide (K136PSSPPEE143)connecting the amino-terminal fragment and protease domains of scuPA that contributes to the binding of uPA fragments to uPAR, inhibits uPA-mediated cell adhesion and retards uPA-mediated metastases. In Specific Aim 1A, we will examine the effects of mutating three residues (K135, K136 and Ser139) in the isolated peptide and in full-length scuPA on binding to uPAR and on cell adhesion. The impact of these mutations on metastasis formation will be examined using tumor cells that co-express human uPAR and plasmin-insensitive scuPA-Glu158. We also observed that Arg137 Arg145 in domain II of uPAR is required for scuPA binding. In Specific Aim IB, we will determine whether Arg137-Arg144 binds scuPA directly or contributes to a composite binding site that involves domain I. Specific Aim 2 is predicated on pilot studies which demonstrate that: a) kringle (K)-IV of plasminogen forms a ternary complex with scuPA-uPAR and inhibits its enzymatic activity; b) apo(a), which contains multiple K-IV repeats, binds to uPAR directly and inhibits cell-associated plasminogen activator activity as well; and c) plasma clearance of Lp(a) is delayed in uPAR-/- mice. In Aim 2A, we will identify molecular determinants in plasminogen K-IV, scuPA and uPAR required to form the ternary complex. In Aim 2B we will examine the binding sites in apo(a) for uPAR and the contribution of uPAR to the deposition of Lp(a) in the vasculature of uPAR uPAR-/-/apo(a)+/+ mice. These studies address newly described interactions between scuPA and its receptor involved in cell adhesion and plasminogen activation and a previous undescribed pathway in which uPAR-mediated enzymatic and adhesive activities are regulated by the kringles of plasminogen and Lp(a).

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

- **Project Title: TACROLIMUS VS INTENSIVE PREDNISONE IN PEDIATRIC FSGS**

  Principal Investigator & Institution: Kaskel, Frederick J.; Developmental Renal and Electrolyte Phys; Montefiore Medical Center (Bronx, Ny) Bronx, Ny 104672490

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-AUG-2007

  Summary: (provided by applicant): Focal Segmental Glomerulosclerosis (FSGS) is a major cause of chronic kidney disease in childhood. This glomerulopaty is more frequent in minority populations, and often recurs in the transplanted kidney. Despite advances particulary in molecular genetics, the cause and optimal treatment of this condition remains poorly defined. Uncontrolled studies in adults with FSGS support the use of prolonged prednisone therapy. Preliminary data in children suggests that the

calcineurin inhibitor tacrolimus may be efficacious in patients who have been refractory to other therapies. The purpose of this multicenter study is to compare the relative efficacy of tacrolimus with that of intensive prednisone therapy in preventing the progression of primary FSGS. This represents the first controlled evaluation of these two promising therapies in children with FSGS. We are proposing a randomized, open-label clinical trial in patients with nephrotic range proteinuria who fail to respond to 4 weeks of oral prednisone and who are found to have FSGS on renal biopsy. Patients will be assigned to receive daily prednisone (60 mg/m2) for 3 months followed by either alternate day prednisone (40 mg/m2) for the ensuing 15 months or tacrolimus plus low-dose alternate day (10 mg/m2) for 18 months. In addition, patients will receive optimal doses of losartan and atorvostatin to control proteinuria, hypertension, and hypelipidemia. The primary outcome indicators will be: complete or partial remission of proteinuria, preservation of glomerular filtration rate, and prevention of renal scarring. Secondary outcome indicators will include correlation of response with a novel histopathologic classification, assessed by a centrol core pathology group. The study design will incorporate collection and storage of potentially important biological samples at the direction of the Data Coordinating Center and the Steering Committee of the NIDDK. The Eastern Regional Group for the Study of Focal Segmental Glomerulosclerosis in Children will be comprised of 41 sites under the direction of the Regional Coordinating Center at Montefiore Medical Center of the Albert Einstein College of Medicine. This project is expected to: 1) improve the outcome of children with FSGS, and, 2) create a nationwide network of clinical investigators that will facilitate future basic and clinical research in the field of pediatric nephrology, in general, and FSGS, in particular.

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

- **Project Title: TESTOSTERONE AND EXERCISE IN MEN AND WOMEN WITH AIDS**

  Principal Investigator & Institution: Klibanski, Anne; Professor of Medicine; Massachusetts General Hospital 55 Fruit St Boston, Ma 02114

  Timing: Fiscal Year 2002; Project Start 30-SEP-1995; Project End 31-AUG-2005

  Summary: (taken from abstract of application) The presentation and course of HIV-infection have changed significantly in the current era of antiviral therapy. Loss of lean body mass and reduced functional capacity occurs in a substantial number of HIV-infected patients, despite protease inhibitor therapy. For such patients, development of effective anabolic strategies is critical to reverse sarcopenia and increase functional capacity. In this proposal, these investigators build upon preliminary data using testosterone and progressive resistance training (PRT) to increase muscle mass and strength in HIV-infected men. They have previously shown potent independent and maximal combined effects of short-term testosterone and PRT in HIV-infected men with wasting and significant sarcopenia. They will now investigate whether long-term PRT effects are maximized by high dose induction anabolic therapy and are sustainable using sequential low dose maintenance testosterone therapy. The development of novel, combined anabolic and PRT strategies is proposed also for women with AIDS wasting, a population with unique body composition changes for whom there are little data. They have previously shown that androgen administration to such patients is safe and, at high doses, results in increased lean body mass. They will assess whether combined androgen and PRT will maximally increase muscle mass and function in HIV-infected women. In addition to muscle loss, a significant percentage of HIV-infected patients experience fat redistribution, characterized by truncal adiposity, and loss of extremity

fat in associate with **hyperlipidemia** and insulin resistance. In preliminary data they have shown significant truncal and visceral adiposity in such patients, which is highly correlated with hyperinsulinemia. Of concern, is that these changes will result in increased long-term cardiovascular morbidity and mortality. The novel use of combined testosterone and aerobic-resistance raining (men) and training alone (women) is proposed for HIV-infected patients with the lipodystrophy syndrome. No therapy as yet exists for this growing population of patients. In this renewal application, they propose: 1) specific resistance training strategies targeted at muscle accrual for HIV-infected men and women in combination with testosterone administration, and 2) development of novel aerobic/anabolic strategies to reverse lipodystrophy. The strategies outlined in this grant proposal will provide critically needed information to optimize muscle mass and function and redistribution of abnormal regional fat deposition among HIV-infected men and women in the new era of HIV-therapy.

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

- **Project Title: THE METABOLIC SYNDROME IN PEDIATRIC OBSTRUCTIVE APNEA**

  Principal Investigator & Institution: Waters, Karen A.; Children's Hospital at Westmead Locked Bag 4001 New South Wales,

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

  Summary: (provided by applicant): This project will evaluate the association between obstructive sleep apnea (OSA) in childhood, and the presence of the "metabolic syndrome". Our aims are: 1. To confirm the association between OSA in children and the presence of known risk factors for future cardiovascular disease. 2. To confirm that the physiological disruptions caused by OSA can induce the same metabolic abnormalities in an animal model, and 3. To confirm that treatment of OSA can reverse the abnormalities underlying the metabolic syndrome. The metabolic syndrome is a combination of hypertension, insulin resistance, and dyslipidemia. The first abnormality to appear in children is insulin resistance. The presence of insulin resistance in children has been associated with development of all three abnormalities in adulthood, and thus with increased risk for later cardiovascular disease. Studying OSA in children provides a unique opportunity to study the mechanisms underlying the association between OSA, the metabolic syndrome, and cardiovascular disease. The majority of children with OSA are NOT obese, so it is possible to determine the relative contribution of factors including obesity, chronic sympathetic activation, and chronic inflammation, if a sufficiently large group is studied. Children who present to a sleep unit already have some combination of symptoms suggestive of OSA. Therefore, a parallel study will seek to understand the earliest associations between OSA and the metabolic syndrome. To do this, piglets will be exposed to repetitive hypercapnic hypoxia, and equivalent studies of metabolic abnormalities will be undertaken. This component of the study will examine the specific sequence of disturbances underlying the metabolic syndrome, with the goal of determining preventative strategies that could be translated into the clinical setting. Finally, children who have OSA will undergo treatment, followed by re-evaluation. If treatment of OSA can reverse the metabolic disturbances present in association with OSA, this will support the need for early and aggressive intervention in childhood OSA.

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

- **Project Title: THE ROLE OF PLTP IN BLP METABOLISM AND ATHEROGENESIS**

  Principal Investigator & Institution: Jiang, Xian-Cheng; Anatomy and Cell Biology; Suny Downstate Medical Center 450 Clarkson Ave New York, Ny 11203

Timing: Fiscal Year 2002; Project Start 15-APR-2002; Project End 31-MAR-2006

Description (provided by applicant): Increased secretion and higher levels of apoB-containing lipoproteins (BLp) are a major cause of the dyslipidemia seen in familial **hyperlipidemia,** obesity, and diabetes. Plasma phospholipid transfer protein (PLTP) is known to mediate transfer of phospholipids between BLp and HDL during their intravascular metabolism, To address a possible role of PLTP in dyslipidemia and atherogenesis, PLTP gene knock-out (PLTPO) mice were bred with differing hyperlipidemic strains. In the apoB transgenic (apoBTg) and apoE knock-out (apoE0) backgrounds, PLTP deficiency resulted in reduced production and levels of BLp, and markedly decreased atherosclerosis. BLp secretion was diminished in hepatocytes from PLTP-deficient mice, an effect that was canceled when PLTP was reintroduced in the adenovirus. Preliminary studies reveal a major and quite unexpected role for PLTP in regulating the secretion of BLp. The biosynthesis of BLp is a two-step process: initial lipidation of apoB occurs in the endoplasmic reticulum, and requires the activity of the microsomal triglyceride transfer protein. A poorly understood, slower second step probably involves the addition of further lipid to the nascent very low-density lipoprotein (VLDL) particle. Our working hypothesis is that PLTP may be involved in the second lipidation step of nascent BLp. Preliminary studies also show that apoB production is not affected in LDL receptor gene knock-out (LDLrO)/PLTPO mice compared with LDLrO mice, but that atherosclerotic lesions are significantly reduced, suggesting that: 1) the influence of PLTP on the production of BLp may require the presence of functional LDL receptors, at least in the liver; and 2) there are some unknown factors, other than lowering BLp, involved in the reduction of atherosclerosis in PLTPO mice. The goal of this project is to investigate further the role of PLTP in BLp metabolism and atherosclerosis. Specific aims are: 1) to evaluate the hypothesis that PLTP may play a role in BLp assembly and secretion in nonlipoprotein-producing model systems (cotransfected by PLTP, apoB, and MTP), primary hepatocyte and hepatoma cells (liver-like cells); 2) to evaluate the hypothesis that PLTP plays a role in BLp assembly and secretion in intestinal cells; and 3) to determine antiatherogenic mechanisms in PLTPO mice other than lowering BLp. This project will provide new information on the relationship between PLTP activity and BLp production, between PLTP activity and atherosclerosis, and will further evaluate PLTP as a therapeutic target.

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

- **Project Title: TISSUE COACTIVATOR AND RECEPTOR EXPRESSION FINGERPRINTS**

  Principal Investigator & Institution: Tsai, Ming-Jer; Charles C. Bell Professor; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

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

  Summary: The major goal of this overall Program Project is to dissect the role of the steroid receptor coactivator (SRC) family in mediating the tissue- selective biological functions of different steroid hormones and their cognate nuclear receptors. (NRs). Our working hypothesis in this Project is that the specificity of coactivator requirement for NRs in target tissues is a function of (i) the intracellular concentrations of coactivators and liganded NRs and (ii) the inherent affinities between specific liganded NR-coactivator pairs. These tissues will be integrated in three Specific Aims. In Specific Aims 1 and 2, we will set out to determine, using multiple tissues and under conditions of ligand induction or withdrawal and in models of the disease states in which NR signaling pathways are implicated, such as type II diabetes, such as type II diabetes, obesity, **hyperlipidemia.** In Specific Aim 3, we will generate data on the patterns of

coactivator selectivity by different NRs by sensitive measurement of the inherent affinities of individual receptor-coactivator pairs using purified receptors. The results we envisage are essential for our understanding of the tissue-specific biology of members of the SRC family. In addition, these studies will pave the way for a greater understanding of the mode of action of selective receptor modulators (SRMs), and will provide prospects for their therapeutic application in the myriad endocrine and metabolic disorders in which NRs and, by association SRCs, are implicated.

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

- **Project Title: TNF-INHIBITOR GENE THERAPY FOR NEOINTIMAL HYPERPLASIA**

  Principal Investigator & Institution: Peppel, Karsten C.; Medicine; Duke University Durham, Nc 27710

  Timing: Fiscal Year 2002; Project Start 01-JUN-2001; Project End 31-MAY-2005

  Summary: Percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG) are each performed on approximately 500,000 patients annually in the US. Both procedures are complicated by activation, migration and proliferation of cells in the vascular wall, leading to neointimal hyperplasia (NH). A preponderance of evidence suggests that the majority of these cells are of vascular smooth muscle origin. NH affects about 30 % of all PCI patients and necessitates reintervention in some 30 % of all CABG cases within two years. The annual cost needed to treat PCI restenosis alone exceeds $2 billion. PCI and saphenous vein CABG surgery both lead to significant injury of the underlying vessel wall, causing endothelial dysfunction and adherence of platelets, neutrophils and circulating cells of the monocyte / macrophage lineage. Locally released cytokines, such as tumor necrosis factor (TNF), synergize with growth factors, including platelet derived growth factor (PDGF) and basic fibroblast growth factor (bFGF), to activate SMCs in the injured vessel segment. In vitro TNF is a strong mitogen for SMCs and can act in concert with PDGF-BB, to stimulate cell growth. This work proposes to examine the contribution of TNF to the activation of SMCs, alone and in combination with various growth factors. To this end mitogen activated protein kinase (MAPK) activation, DNA synthesis, proliferation, chemotaxis and apoptosis will be examined in TNF treated and untreated SMCs. In addition, this proposal seeks to test the hypothesis that inhibition of TNF can decrease the degree of SMC activation in vitro and can reduce the size of neointima formation in vivo in an experimental animal model. To inhibit TNF, a chimeric TNF receptor extracellular domain - murine immunoglobulin heavy chain construct (TNF-I) was generated and inserted into a recombinant adenovirus (rec. AD-TNF-I). This virus will be used to infect rabbit jugular veins ex vivo that will be grafted across the rabbit's carotid artery in a well characterized model of neointima hyperplasia. Four weeks after bypass grafting the degree of neointima formation in rec.AD-TNF-I and rec.AD-control infected veins will be measured histologically. This will be done both in rabbits receiving a normal diet and also in animals given a high fat diet to examine the contribution of **hyperlipidemia** towards the development of neointimal hyperplasia in this setting. Reduction of vein graft neointimal hyperplasia by inhibition of TNF may have significant therapeutic implications for human vascular diseases.

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

- **Project Title: VASCULAR FUNCTION BY MAGNETIC RESONANCE ANGIOGRAPHY**

  Principal Investigator & Institution: Silber, Harry A.; Medicine; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2002; Project Start 13-AUG-2001; Project End 31-JUL-2006

  Summary: It is unclear why individuals at risk for atherosclerosis develop more severe disease in some vascular beds than others, e.g. femoral arteries tend to develop much more severe disease than do brachial arteries. We hypothesize that these different susceptibilities are associated with regional differences in vascular endothelial function within those individuals. Wall shear stress is considered to be the primary hemodynamic stimulus for endothelial activity. Therefore, comparing the relationship between wall shear stress stimulus and endothelial response in different vascular beds may allow the evaluation of regional differences in endothelial function. Using phase-contrast magnetic resonance angiography, we have shown a linear relationship between wall shear stress during peak reactive hyperemia and resulting vessel dilatation in normal brachial arteries. We have also developed another method to assess endothelial stimulus response relationship by evaluating the time-course of endothelial regulation of wall shear stress following post-ischemic hyperemia, and a technique to assess circumferential distribution of wall shear stress in a single arterial cross-section. The aims of this project are 1) to determine whether the endothelial stimulus-response relationships are altered in the presence of cardiovascular risk factors and in the presence of vascular disease, 2) to determine whether the relationships are sensitive to changes in endothelial function after a 6-week course of an HMG-Co A reductase inhibitor in subjects with **hyperlipidemia,** and 3) to determine whether the relationships or the circumferential stress distribution differ in different vascular beds. The investigators anticipate that this study will improve the ability to distinguish between normal and impaired endothelial function, and will enhance the understanding of atherosclerosis development. The proposal will involve mentorship, training, and resources from cardiovascular clinical research experts and several world-renown divisions of Johns Hopkins: Cardiovascular MRI, Biomedical Engineering, and The School of Public Health. The mentors, collaborators, environment, and research plan are ideal for achieving the applicant's long-term goal of becoming an independent clinical investigator, applying innovative engineering techniques toward patient-oriented cardiovascular problems.

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

- **Project Title: VASCULAR INFLAMMATION AND ADVANCED GLYCATION ENDPRODUCTS**

  Principal Investigator & Institution: Taylor, W Robert.; Associate Professor; Medicine; Emory University 1784 North Decatur Road Atlanta, Ga 30322

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

  Summary: (provided by applicant): The leading cause of morbidity and mortality in both insulin-dependent diabetes mellitus (IDDM) and non-insulin-dependent diabetes mellitus (NIDDM) is atherosclerotic cardiovascular disease. The age-adjusted incidence of myocardial infarction is six times greater in diabetic men, and four times greater in diabetic women than in nondiabetic subjects. This markedly accelerated vascular pathology cannot be fully explained by the well-described coexistence of traditional cardiovascular risk factors. Although the association of chronic hyperglycemia and diabetic micro- and macrovascular disease has been established, the mechanisms of the

linkage between hyperglycemia and atherosclerotic vascular pathology have not yet been fully elucidated. Diabetes, as a disease state, presents a potentially very complex metabolic stimulus to the cellular components of the arterial wall. The functionally relevant components of the altered metabolic milieu of diabetes include not only changes in glucose and insulin levels, but may also include "secondary" metabolic abnormalities that occur as a result of the primary abnormalities in insulin and glucose metabolism. Advanced glycation endproducts (AGEs) are the late products of the modification of proteins, lipids and nucleic acids by reducing sugars. They have been implicated as an important component of the metabolic abnormalities resulting in diabetic vasculopathy. The central hypothesis of this proposal is that AGEs have an important, and potentially central, role in the accelerated vasculopathy of NIDDM and IDDM via the regulation of redox-sensitive proinflammatory cell signaling pathways. The proposed studies will systematically explore AGE-mediated regulation of redox state and proinflammatory gene products in vascular disease and determine the functionally relevant molecular events responsible for the proatherogenic effects in-vivo.

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

- **Project Title: VASCULAR MECHANISMS IN ATHEROGENESIS**

  Principal Investigator & Institution: Heistad, Donald D.; Director; Internal Medicine; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 01-JUN-2000; Project End 31-MAY-2005

  Summary: Impairment of endothelial function, which is a hallmark of atherosclerosis in experimental animal and humans, may contribute to development of atherosclerosis and its complications. The overall theme of this Program is mechanisms of dysfunction of endothelium and vascular muscle in atherogenesis. The investigators propose to integrated physiological and molecular approaches to examine mechanisms by which risk factors and oxidants may produce atherosclerosis. The Program consists of three projects and an administrative core. Project 1 tests the hypothesis that angiotensin II contributes to increased levels of superoxide in blood vessels and that this mechanism may contribute to acceleration of atherosclerosis by hypertension. Two novel hypertensive transgenic mice have been made to test this hypothesis. Circulating levels of angiotensin II are markedly elevated in one model, and normal in the other model; the degree of hypertension, however, is similar in the two models. These models will allow a new approach to examine the role of angiotensin in vascular changes during hypertension and atherosclerosis. The investigators in Project 2 have reported recently that, in contrast to previous studies which have focused on the role of reactive oxygen species (ROS) generated by endothelium, vascular muscle is a major source of superoxide in atherosclerotic vessels. Studies are proposed to determine the important of, and examine enzymatic mechanisms that account for, production of superoxide by smooth muscle in atherosclerotic vessels. Studies are proposed to determine the importance of, and examine enzymatic mechanisms that account for, production of superoxide smooth muscle in atherosclerotic vessels. Studies are planned in a genetic model of atherosclerosis in mice, and in a primate model of atherosclerosis and repression. Project 3 proposes to test the hypothesis that excessive production of ROS may regulate both proliferation and promote death of smooth muscle cells. Gene transfer approaches will be used to directly increase concentration of antioxidant enzymes, rather than using topical application of the enzymes, Studies are planned to determine whether endogenous H2O2, and the balance between superoxide and H2O2, regulate both proliferation and viability of smooth muscle cells. The studies will examine mechanisms that account for enhanced susceptibility of neointimal smooth

muscle cells to cytotoxicity by RO2. Target goals of the Program include clarification include clarification of mechanisms by which risk factors produce atherosclerosis, insight into cellular and enzymatic sources of reactive oxygen species in atherosclerotic vessels, and better understanding of potential therapeutic targets, including oxidative processes, angiotensin II, and **hyperlipidemia.**

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

- **Project Title: WHY DO METABOLIC RISK FACTORS CLUSTER WITH HYPERTENSION?**

  Principal Investigator & Institution: Kurtz, Theodore W.; Professor; Laboratory Medicine; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002; Project Start 20-SEP-2000; Project End 31-JUL-2004

  Summary: (Adapted from the application) Insulin resistance has been frequently observed in patients with essential hypertension, although the mechanisms responsible for the hypertension "metabolic syndrome" and clustering of cardiovascular risk factors remain poorly understood. Evidence from both family studies and experimental animals indicates that genetic risk factors may play a significant role in the clustering of cardiovascular risk factors. The spontaneously hypertensive rat (SHR), a widely studied experimental animal model of human essential hypertension, also demonstrates increased plasma insulin levels and insulin resistance when compared with other strains with low blood pressure. The PI and her collaborators have derived a novel SHR congenic strain that provides an opportunity to investigate the clustering of hypertension and insulin resistance. By transferring a piece of chromosome 4 from the normotensive Brown Norway rat onto the genetic background of the SHR rat, the applicant has bracketed a specific chromosomal segment approximately 37 cM in size, that improves both blood pressure and insulin resistance in the SHR. This segment also contains the Cd36 gene, which encodes a fatty acid transporter that was previously thought to be a candidate in the pathogenesis of insulin resistance and blood pressure. The PI proposes to use meiotic mapping in an interval specific segregating population to narrowly map the blood pressure locus on chromosome 4, derive a congenic subline that carries the relevant segment of chromosome 4 and test the potential role of Cd36 in blood pressure control and insulin resistance in transgenic SHR by overexpressing this gene.

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

- **Project Title: XANTHINE OXIDASE AND VASCULAR DYSFUNCTION**

  Principal Investigator & Institution: White, C Roger.; Associate Professor; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2002; Project Start 01-JUN-1998; Project End 31-MAY-2003

  Summary: (Adapted from applicants' abstract) Reactive oxygen species induce changes in vascular function in conditions such as stroke, hypertension and atherosclerosis. The nature and complexity of lesion development in atherosclerosis suggest that the disease may have several etiologies. The generation of free radicals is associated with alterations in both vascular reactivity and lipoprotein metabolism. The studies proposed in this application are designed to provide new information concerning oxidant-induced damage in the vessel wall. It is hypothesized that impaired blood vessel function in hypercholesterolemic rabbits is due to the modification of nitric oxide (NO) by superoxide anion (O2-), leading to the production of the potent oxidant peroxynitrite

(ONOO-). Reactive oxygen species are generated under normal physiological conditions, with native antioxidant scavengers minimizing oxidant-mediated injury. An imbalance in antioxidant defense mechanisms and changes in cellular metabolic processes then contributes to the development and progression of atherosclerotic disease. The studies outlined in this application are designed to provide new information describing the cellular mechanisms involved in these free radical reactions, namely that free radical injury in blood vessels of hypercholesterolemic rabbits is linked to the binding and concentration of xanthine oxidase (XO) at glycosaminoglycan (GAG) sites on the surface of endothelial cells and in the interstitial space. The hypothesis to be tested in this application is that GAG-bound XO is an important source of O2-, thus ONOO- formation, and contributes to the oxidative component of hypercholesterolemia. GAG function or expression may be altered by **hyperlipidemia,** thereby facilitating incorporation of lipoproteins in the vessel wall as well as serving as a site for XO binding and incorporation, influencing changes in the vasculature and playing an important role in the pathological events associated with hyper-cholesterolemia. (End of Abstract)

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

- **A Mutation in the Promoter of the Lipoprotein Lipase (LPL) Gene in a Patient with Familial Combined Hyperlipidemia and Low LPL Activity.** by Yang W, Nevin DN, Peng R, Brunzell JD, Deeb SS.; 1995 May 9; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=41964
- **Chlamydia pneumoniae and Hyperlipidemia Are Co-Risk Factors for Atherosclerosis: Infection Prior to Induction of Hyperlipidemia Does Not Accelerate Development of Atherosclerotic Lesions in C57BL/6J Mice.** by Blessing E, Campbell LA, Rosenfeld ME, Kuo CC.; 2002 Sep; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=128267

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

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

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

- **Immune complex hyperlipidemia induced by an apolipoprotein-reactive immunoglobulin A paraprotein from a patient with multiple myeloma. Characterization of this immunoglobulin.** by Kilgore LL, Patterson BW, Parenti DM, Fisher WR.; 1985 Jul;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=423752
- **Lamellar lipoproteins uniquely contribute to hyperlipidemia in mice doubly deficient in apolipoprotein E and hepatic lipase.** by Bergeron N, Kotite L, Verges M, Blanche P, Hamilton RL, Krauss RM, Bensadoun A, Havel RJ.; 1998 Dec 22;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=28098
- **Proteinuria, not altered albumin metabolism, affects hyperlipidemia in the nephrotic rat.** by Davies RW, Staprans I, Hutchison FN, Kaysen GA.; 1990 Aug;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=296766
- **Temporary amelioration of hyperlipidemia in low density lipoprotein receptor-deficient rabbits transplanted with genetically modified hepatocytes.** by Wilson JM, Chowdhury NR, Grossman M, Wajsman R, Epstein A, Mulligan RC, Chowdhury JR.; 1990 Nov;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=54971

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

- **A case of severe hyperlipidemia caused by long-term tube feedings.**
  Author(s): Tanaka S, Miki T, Hsieh ST, Kim JI, Yasumoto T, Taniguchi T, Ishikawa Y, Yokoyama M.
  Source: J Atheroscler Thromb. 2003; 10(5): 321-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14718750

[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 patient with hyperlipidemia who had a gallbladder stone caused by administration of fenofibrate.**
  Author(s): Inuzuka S, Tomiyasu N, Kumamoto M, Egashira T, Kinoshita J, Shishido S, Sata M, Ueno T.
  Source: Kurume Med J. 2003; 50(1-2): 77-80.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12971269

- **A retrospective cohort study of correlates of response to pharmacologic therapy for hyperlipidemia in members of a managed care organization.**
  Author(s): Valuck RJ, Williams SA, MacArthur M, Saseen JJ, Nair KV, McCollum M, Endor JE.
  Source: Clinical Therapeutics. 2003 November; 25(11): 2936-57.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14693317

- **A statin for a patient with hyperlipidemia and hepatitis C?**
  Author(s): Nash DT.
  Source: Postgraduate Medicine. 2004 May; 115(5): 86.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15171081

- **Abdominal obesity and dyslipidemia in the metabolic syndrome: importance of type 2 diabetes and familial combined hyperlipidemia in coronary artery disease risk.**
  Author(s): Carr MC, Brunzell JD.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2004 June; 89(6): 2601-7. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15181030

- **Alcohol consumption had no beneficial effect on serum lipids in a substantial proportion of patients with primary hyperlipidemia.**
  Author(s): Sijbrands EJ, Smelt AH.
  Source: Journal of Clinical Epidemiology. 2000 October; 53(10): 1020-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11027934

- **Alterations of HDL subclasses in hyperlipidemia.**
  Author(s): Xu Y, Fu M.
  Source: Clinica Chimica Acta; International Journal of Clinical Chemistry. 2003 June; 332(1-2): 95-102.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12763286

- **An assessment of the independent effects of olanzapine and risperidone exposure on the risk of hyperlipidemia in schizophrenic patients.**
  Author(s): Koro CE, Fedder DO, L'Italien GJ, Weiss S, Magder LS, Kreyenbuhl J, Revicki D, Buchanan RW.
  Source: Archives of General Psychiatry. 2002 November; 59(11): 1021-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12418935

- **An ounce of prevention. Drugs used to treat hyperlipidemia (Part 1).**
  Author(s): Turkoski BB.
  Source: Orthopaedic Nursing / National Association of Orthopaedic Nurses. 2004 January-February; 23(1): 58-61. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14999954

- **An ounce of prevention. Drugs used to treat hyperlipidemia (Part 2).**
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  Source: Medsurg Nursing : Official Journal of the Academy of Medical-Surgical Nurses. 1994 August; 3(4): 319-21.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7920858

- **Undertreatment of hyperlipidemia in patients with coronary artery disease and heart failure.**
  Author(s): Sueta CA, Massing MW, Chowdhury M, Biggs DP, Simpson RJ Jr.
  Source: Journal of Cardiac Failure. 2003 February; 9(1): 36-41.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12612871

- **Undertreatment of hyperlipidemia in the secondary prevention of coronary artery disease.**
  Author(s): Majumdar SR, Gurwitz JH, Soumerai SB.
  Source: Journal of General Internal Medicine : Official Journal of the Society for Research and Education in Primary Care Internal Medicine. 1999 December; 14(12): 711-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10632815

- **Uremic hyperlipidemia: the nature of the problem.**
  Author(s): Sherrard DJ, Brunzell JD.
  Source: Proc Clin Dial Transplant Forum. 1977; 7: 176-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=210447

- **Use of an electronic medical record in disease management programs: a case study in hyperlipidemia.**
  Author(s): Hunt J, Siemienczuk J, Erstgaard P, Slater J, Middleton B.
  Source: Medinfo. 2001; 10(Pt 1): 825-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11604850

- **Use of cholestyramine in the treatment of children with familial combined hyperlipidemia.**
  Author(s): Liacouras CA, Coates PM, Gallagher PR, Cortner JA.
  Source: The Journal of Pediatrics. 1993 March; 122(3): 477-82.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8441109

- **Use of fibrates in the management of hyperlipidemia in HIV-infected patients receiving HAART.**
  Author(s): Calza L, Manfredi R, Chiodo F.
  Source: Infection. 2002 January; 30(1): 26-31.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11876511

- **Use of niacin in the prevention and management of hyperlipidemia.**
  Author(s): Robinson AW, Sloan HL, Arnold G.
  Source: Progress in Cardiovascular Nursing. 2001 Winter; 16(1): 14-20. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11252872

- **Use of niacin, statins, and resins in patients with combined hyperlipidemia.**
  Author(s): Brown BG, Zambon A, Poulin D, Rocha A, Maher VM, Davis JW, Albers JJ, Brunzell JD.
  Source: The American Journal of Cardiology. 1998 February 26; 81(4A): 52B-59B. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9526815

- **Use of simvastatin treatment in patients with combined hyperlipidemia in clinical practice. For the Simvastatin Combined Hyperlipidemia Registry Group.**
  Author(s): Vicari RM, Wan GJ, Aura AM, Alexander CM, Markson LE, Teutsch SM.
  Source: Archives of Family Medicine. 2000 September-October; 9(9): 898-905.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11031398

- **Value and safety of diet modification to control hyperlipidemia in childhood and adolescence. A statement for physicians. Ad Hoc Committee of the Steering Committee for Medical and Community Program of the American Heart Association.**
  Author(s): Glueck CJ, McGill HC Jr, Shank RE, Lauer RM.
  Source: Circulation. 1978 August; 58(2): 381A-385A.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=668092

- **Variable influence of statins on isoprostanes in hyperlipidemia.**
  Author(s): Sinzinger H, Oguogho A.
  Source: Advances in Experimental Medicine and Biology. 2003; 525: 209-12.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12751770

- **Variants in the PPARgamma gene affect fatty acid and glycerol metabolism in familial combined hyperlipidemia.**
  Author(s): Eurlings PM, van der Kallen CJ, Vermeulen VM, de Bruin TW.
  Source: Molecular Genetics and Metabolism. 2003 November; 80(3): 296-301.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14680975

- **Variation in the apo AI/CIII/AIV gene complex: its association with hyperlipidemia.**
  Author(s): Shoulders CC, Ball MJ, Baralle FE.
  Source: Atherosclerosis. 1989 December; 80(2): 111-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2514696

- **Vestibular vertigo associated with hyperlipidemia: response to antilipidemic therapy.**
  Author(s): Saadah HA.
  Source: Archives of Internal Medicine. 1993 August 9; 153(15): 1846, 1849.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8333820

- **Vitamin A is linked to the expression of the AI-CIII-AIV gene cluster in familial combined hyperlipidemia.**
  Author(s): Ribalta J, Girona J, Vallve JC, La Ville AE, Heras M, Masana L.
  Source: Journal of Lipid Research. 1999 March; 40(3): 426-31.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10064730

- **What a dietitian should know about hyperlipidemia.**
  Author(s): Brown HB, Farrand M.
  Source: Journal of the American Dietetic Association. 1973 August; 63(2): 169-70.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=4352329

- **What ALLHAT tells us about treating high-risk patients with hypertension and hyperlipidemia.**
  Author(s): Geraci TS, Geraci SA.
  Source: The Journal of Cardiovascular Nursing. 2003 November-December; 18(5): 389-95. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14680343

- **What's new: arguments for and against the treatment of hyperlipidemia.**
  Author(s): Gotto AM Jr, Wittels EH.
  Source: Tex Med. 1980 September; 76(9): 38-42. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7434247

- **When and how to treat hyperlipidemia.**
  Author(s): Kuo PT.
  Source: Primary Care. 1985 March; 12(1): 77-89.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3873080

- **When to treat hyperlipidemia.**
  Author(s): Kane JP, Malloy MJ.
  Source: Adv Intern Med. 1988; 33: 143-63. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3278503

- **Xanthelasma palpebrum--a marker for hyperlipidemia in NIDDM patients?**
  Author(s): Premalatha G, Mohan V.
  Source: J Assoc Physicians India. 1996 January; 44(1): 73-4. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8773112

- **Xanthoma of bone: first sign of hyperlipidemia type IIB: a case report.**
  Author(s): Dallari D, Marinelli A, Pellacani A, Valeriani L, Lesi C, Bertoni F, Giunti A.
  Source: Clinical Orthopaedics and Related Research. 2003 May; (410): 274-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12771840

- **Xanthoma of the liver in a patient with multiple myeloma associated with hyperlipidemia. A case report.**
  Author(s): Yim H, Ahn HJ, Park C, Cheon JY.
  Source: Journal of Korean Medical Science. 1995 December; 10(6): 453-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8924232

- **Xanthomas and hyperlipidemia in a human immunodeficiency virus-infected child receivng highly active antiretroviral therapy.**
  Author(s): Babl FE, Regan AM, Pelton SI.
  Source: The Pediatric Infectious Disease Journal. 2002 March; 21(3): 259-60.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12005095

- **Xanthomatized atypical T cells in a patient with mycosis fungoides and hyperlipidemia.**
  Author(s): Ross EV, Roman L, Rushin JM, Cobb MW, Friedman KJ.
  Source: Archives of Dermatology. 1992 November; 128(11): 1499-502.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1332629

- **Xanthomatosis with minimal hyperlipidemia.**
  Author(s): Shakir KM, Larocque JC, Reed LH, O'Brian JT.
  Source: Military Medicine. 1987 December; 152(12): 641-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3122098

- **Xanthomatous neuropathy associated with hyperlipidemia.**
  Author(s): Ludwig J.
  Source: Human Pathology. 1994 February; 25(2): 215.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8119725

- **XbaI polymorphism of the apolipoprotein B gene in patients with hyperlipidemia and echo-Doppler evidence of arterial lesions.**
  Author(s): De Lorenzo F, Rubba P, Monticelli A, Cortese C, Bond HM, De Simone B, Mastranzo P, Perrotta A, Mossetti G, Cocozza S.
  Source: Artery. 1993; 20(2): 103-14.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8512457

CHAPTER 2. NUTRITION AND HYPERLIPIDEMIA

Overview

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

Finding Nutrition Studies on Hyperlipidemia

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

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

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

- **A diet containing food rich in soluble and insoluble fiber improves glycemic control and reduces hyperlipidemia among patients with type 2 diabetes mellitus.**
  Author(s): Department of Nutrition and Foodservice Systems, The University of North Carolina at Greensboro, 27402-6170, USA.
  Source: McIntosh, M Miller, C Nutr-Revolume 2001 February; 59(2): 52-5 0029-6643
- **Effects of gemfibrozil on triglyceride levels in patients with NIDDM. Hyperlipidemia in Diabetes Investigators.**
  Author(s): Eastern Virginia Medical School, Department of Internal Medicine, Norfolk 23510.
  Source: Vinik, A I Colwell, J A Diabetes-Care. 1993 January; 16(1): 37-44 0149-5992
- **Nutrition management of hyperlipidemia and diabetes.**
  Source: Worthington Roberts, B. Food-Nutr-News. Chicago, Ill. : National Live Stock and Meat Board. Sept/October 1987. volume 59 (4) page 67-69. ill. 0015-6310
- **Obesity, diabetes, and hyperlipidemia in a central Australian aboriginal community with a long history of acculturation.**
  Author(s): Department of Human Nutrition, Deakin University, Geelong, Victoria, Australia.
  Source: O'Dea, K Patel, M Kubisch, D Hopper, J Traianedes, K Diabetes-Care. 1993 July; 16(7): 1004-10 0149-5992
- **Remission of proteinuria following correction of hyperlipidemia in NIDDM patients with nondiabetic glomerulopathy.**
  Author(s): Service de Medecine Interne, Hopital Lariboisiere, Paris, France.
  Source: Dubois, D Chanson, P Timsit, J Chauveau, D Nochy, D Guillausseau, P J Lubetzki, J Diabetes-Care. 1994 August; 17(8): 906-8 0149-5992
- **Treatment of hypercholesterolemia and combined hyperlipidemia with simvastatin and gemfibrozil in patients with NIDDM. A multicenter comparison study.**
  Author(s): Department of Medicine, University of Helsinki, Finland.
  Source: Tikkanen, M J Laakso, M Ilmonen, M Helve, E Kaarsalo, E Kilkki, E Saltevo, J Diabetes-Care. 1998 April; 21(4): 477-81 0149-5992

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

- **A comparative study on the beneficial effects of garlic (Allium sativum Linn), amla (Emblica Officinalis Gaertn)and onion (Allium cepa Linn) on the hyperlipidemia induced by butter fat and beef fat in rats.**
  Author(s): Department of Medical Biochemistry, School of Medical Education, M.G. University, Kottayam, India.
  Source: Augusti, K T Arathy, S L Asha, R Ramakrishanan, J Zaira, J Lekha, V Smitha, S Vijayasree, V M Indian-J-Exp-Biol. 2001 Aug; 39(8): 760-6 0019-5189
- **Contemporary management of hyperlipidemia in women.**
  Author(s): Preventive Cardiology Program, New York Presbyterian Hospital, Columbia University College of Physicians and Surgeons, New York, NY10032, USA. ljm10@columbia.edu
  Source: Mosca, L J J-Womens-Health-Gend-Based-Med. 2002 June; 11(5): 423-32 1524-6094

- **Experimental arterial thrombosis in genetically or diet induced hyperlipidemia in rats--role of vitamin K-dependent clotting factors and prevention by low-intensity oral anticoagulation.**
  Author(s): Angela Valenti Laboratory of Genetic and Environmental Risk Factors for Thrombotic Disease, Consorzio Mario Negri Sud, Santa Maria Imbaro, Italy.
  Source: De Curtis, A D'Adamo, M C Amore, C Polishchuck, R Castelnuovo, A D Donati, M B Iacoviello, L Thromb-Haemost. 2001 December; 86(6): 1440-8 0340-6245
- **Should pediatric patients with hyperlipidemia receive drug therapy?**
  Author(s): The Royal Oldham Hospital, Oldham, and Manchester Royal Infirmary, Manchester, United Kingdom. D.Bhatnagar@man.ac.uk
  Source: Bhatnagar, D Paediatr-Drugs. 2002; 4(4): 223-30 1174-5878
- **The effects of an instant haw beverage on lipid levels, antioxidant enzyme and immune function in hyperlipidemia patients.**
  Author(s): Institute of Sports Medicine, The Third Hospital, Peking University, Beijing 100083, China.
  Source: Chen, J Xue, B Li, K Shi, J Krempin, D Zhu, M Garland, C Zhonghua-Yu-Fang-Yi-Xue-Za-Zhi. 2002 May; 36(3): 172-5 0253-9624

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 hyperlipidemia; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **Vitamins**

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

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

  Niacin
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,892,00.html

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

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

  Pantothenic Acid and Pantethine
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Vitamin B12
  Source: Prima Communications, Inc.www.personalhealthzone.com

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

Vitamin B3
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

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

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

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

- **Minerals**

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

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

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

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

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

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

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

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

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

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

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

L-Carnitine
Source: Healthnotes, Inc.; www.healthnotes.com

Lecithin/Phosphatidylcholine/Choline
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

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

Vanadium
Alternative names: Vanadate, Vanadyl
Source: Integrative Medicine Communications; www.drkoop.com

- **Food and Diet**

Artichoke
Alternative names: Cynara scolymus
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

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

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

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

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

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

Garlic
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,786,00.html

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

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

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

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

Lobster & Crayfish
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/foods_view/0,1523,175,00.html

Low-Fat Diet
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

Shiitake Mushrooms
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/foods_view/0,1523,308,00.html

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

Soy Products
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/foods_view/0,1523,135,00.html

Soybeans
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/foods_view/0,1523,105,00.html

Special Diets Index
Source: Healthnotes, Inc.; www.healthnotes.com

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

Trans-Fats
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

CHAPTER 3. ALTERNATIVE MEDICINE AND HYPERLIPIDEMIA

Overview

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

- **A comparative study on the beneficial effects of garlic (Allium sativum Linn), amla (Emblica Officinalis Gaertn)and onion (Allium cepa Linn) on the hyperlipidemia induced by butter fat and beef fat in rats.**
  Author(s): Augusti KT, Arathy SL, Asha R, Ramakrishanan J, Zaira J, Lekha V, Smitha S, Vijayasree VM.
  Source: Indian J Exp Biol. 2001 August; 39(8): 760-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12018576

- **A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial.**
  Author(s): Yancy WS Jr, Olsen MK, Guyton JR, Bakst RP, Westman EC.
  Source: Annals of Internal Medicine. 2004 May 18; 140(10): 769-77.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15148063

- **Acute hyperlipidemia increases oxidative stress more in African Americans than in white Americans.**
  Author(s): Lopes HF, Morrow JD, Stojiljkovic MP, Goodfriend TL, Egan BM, Stoijiljkovic MP.
  Source: American Journal of Hypertension : Journal of the American Society of Hypertension. 2003 May; 16(5 Pt 1): 331-6. Erratum In: Am J Hypertens. 2003 December; 16(12): 1083. Stoijiljkovic Milos P [corrected to Stojiljkovic Milos P].
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12745192

- **An omega-3 polyunsaturated fatty acid concentrate increases plasma high-density lipoprotein 2 cholesterol and paraoxonase levels in patients with familial combined hyperlipidemia.**
  Author(s): Calabresi L, Villa B, Canavesi M, Sirtori CR, James RW, Bernini F, Franceschini G.
  Source: Metabolism: Clinical and Experimental. 2004 February; 53(2): 153-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14767865

- **Astragalus mongholicus and Angelica sinensis compound alleviates nephrotic hyperlipidemia in rats.**
  Author(s): Li J, Yu L, Li N, Wang H.
  Source: Chinese Medical Journal. 2000 April; 113(4): 310-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11775225

- **Cardiovascular effects of milk enriched with omega-3 polyunsaturated fatty acids, oleic acid, folic acid, and vitamins E and B6 in volunteers with mild hyperlipidemia.**
  Author(s): Carrero JJ, Baro L, Fonolla J, Gonzalez-Santiago M, Martinez-Ferez A, Castillo R, Jimenez J, Boza JJ, Lopez-Huertas E.
  Source: Nutrition (Burbank, Los Angeles County, Calif.). 2004 June; 20(6): 521-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15165614

- **Cholesterol lowering effect of SG-GN3, the extract of salted and fermented small shrimps, Acetes japonicus, in Triton WR-1339 or high cholesterol-diet induced hypercholesterolemic rats.**
  Author(s): Seok SH, Park JH, Cho SA, Choi SA, Park JH.
  Source: Journal of Ethnopharmacology. 2004 April; 91(2-3): 231-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15120444

- **Comparative effects of curcumin and photo-irradiated curcumin on alcohol- and polyunsaturated fatty acid-induced hyperlipidemia.**
  Author(s): Rukkumani R, Sri Balasubashini M, Vishwanathan P, Menon VP.
  Source: Pharmacological Research : the Official Journal of the Italian Pharmacological Society. 2002 September; 46(3): 257-64.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12220969

- **Contemporary management of hyperlipidemia in women.**
  Author(s): Mosca LJ.
  Source: Journal of Women's Health & Gender-Based Medicine. 2002 June; 11(5): 423-32. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12165159

- **Drug treatment of combined hyperlipidemia.**
  Author(s): Wierzbicki AS, Mikhailidis DP, Wray R.
  Source: American Journal of Cardiovascular Drugs : Drugs, Devices, and Other Interventions. 2001; 1(5): 327-36. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14728015

- **Eating behaviors of elderly persons with hyperlipidemia in urban Chiang Mai.**
  Author(s): Aree P, Tanphaichitr V, Suttharangsri W, Kavanagh K.
  Source: Nursing & Health Sciences. 2004 March; 6(1): 51-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14764194

- **Effect of prickly pear (Opuntia robusta) on glucose- and lipid-metabolism in non-diabetics with hyperlipidemia--a pilot study.**
  Author(s): Wolfram RM, Kritz H, Efthimiou Y, Stomatopoulos J, Sinzinger H.
  Source: Wiener Klinische Wochenschrift. 2002 October 31; 114(19-20): 840-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12503475

- **Effect of statin therapy on remnant lipoprotein cholesterol levels in patients with combined hyperlipidemia.**
  Author(s): Stein DT, Devaraj S, Balis D, Adams-Huet B, Jialal I.
  Source: Arteriosclerosis, Thrombosis, and Vascular Biology. 2001 December; 21(12): 2026-31.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11742880

- **Effects of dietary powdered green tea and theanine on tumor growth and endogenous hyperlipidemia in hepatoma-bearing rats.**
  Author(s): Zhang G, Miura Y, Yagasaki K.
  Source: Bioscience, Biotechnology, and Biochemistry. 2002 April; 66(4): 711-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12036040

- **Effects of gamichunggantang on hyperlipidemia.**
  Author(s): Son CG, Choi WJ, Shin JW, Han SH, Cho JH, Song KC, Cho CK.
  Source: Acta Pharmacologica Sinica. 2003 February; 24(2): 133-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12546720

- **Effects of peroxidase on hyperlipidemia in mice.**
  Author(s): Wang L, Wei L, Wang L, Xu C.

Source: Journal of Agricultural and Food Chemistry. 2002 February 13; 50(4): 868-70.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11829659

- **Genetically defined hyperlipidemia.**
  Author(s): Smit JW, Diamant M.
  Source: Pharmacogenomics. 2004 April; 5(3): 295-304. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15102544

- **Hawthorn fruit is hypolipidemic in rabbits fed a high cholesterol diet.**
  Author(s): Zhang Z, Ho WK, Huang Y, James AE, Lam LW, Chen ZY.
  Source: The Journal of Nutrition. 2002 January; 132(1): 5-10.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11773500

- **High density lipoprotein-cholesterol changes in children with high cholesterol levels at birth.**
  Author(s): Bastida S, Sanchez-Muniz FJ, Cuena R, Perea S, Aragones A.
  Source: European Journal of Pediatrics. 2002 February; 161(2): 94-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11954759

- **Management of hyperlipidemia.**
  Author(s): Dog TL, Riley D.
  Source: Alternative Therapies in Health and Medicine. 2003 May-June; 9(3): 28-40; Quiz 41. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12776473

- **Should pediatric patients with hyperlipidemia receive drug therapy?**
  Author(s): Bhatnagar D.
  Source: Paediatric Drugs. 2002; 4(4): 223-30. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11960511

- **Sopungsungi-won (SP) prevents the onset of hyperglycemia and hyperlipidemia in Zucker diabetic fatty rats.**
  Author(s): Kim YY, Kang HJ, Ko SK, Chung SH.
  Source: Arch Pharm Res. 2002 December; 25(6): 923-31.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12510849

- **Soy isoflavones prevent ovariectomy-induced atherosclerotic lesions in Golden Syrian hamster model of postmenopausal hyperlipidemia.**
  Author(s): Lucas EA, Lightfoot SA, Hammond LJ, Devareddy L, Khalil DA, Daggy BP, Soung do Y, Arjmandi BH.

Source: Menopause (New York, N.Y.). 2003 July-August; 10(4): 314-21.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12851514

- **Statin-fibrate combination: therapy for hyperlipidemia: a review.**
  Author(s): Wierzbicki AS, Mikhailidis DP, Wray R, Schacter M, Cramb R, Simpson WG, Byrne CB.
  Source: Current Medical Research and Opinion. 2003; 19(3): 155-68. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12814127

- **The effects of an instant haw beverage on lipid levels, antioxidant enzyme and immune function in hyperlipidemia patients.**
  Author(s): Chen J, Xue B, Li K, Shi J, Krempin D, Zhu M, Garland C.
  Source: Zhonghua Yu Fang Yi Xue Za Zhi. 2002 May; 36(3): 172-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12410950

- **Treatment of hyperlipidemia.**
  Author(s): Henley E, Chang L, Hollander S.
  Source: The Journal of Family Practice. 2002 April; 51(4): 370-6. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11978263

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 hyperlipidemia; 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**

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

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

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

  Atherosclerosis and Heart Disease Prevention
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Cardiovascular Disease Overview
  Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

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

  Heart Attack
  Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

Hypertension
Alternative names: High Blood Pressure
Source: Prima Communications, Inc.www.personalhealthzone.com

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

Insulin Resistance Syndrome
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

Myocardial Infarction
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

Transient Ischemic Attacks
Source: Integrative Medicine Communications; www.drkoop.com

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

- **Alternative Therapy**

Ayurveda
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,672,00.html

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

Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,709,00.html

- **Herbs and Supplements**

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

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

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

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

Beni-Koji
Source: Integrative Medicine Communications; www.drkoop.com

Beta-Sitosterol
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,972,00.html

Bile Acid Sequestrants
Source: Healthnotes, Inc.; www.healthnotes.com

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

Carotenoids
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,763,00.html

Chinese Scullcap
Alternative names: Scutellaria baicalensis
Source: Healthnotes, Inc.; www.healthnotes.com

Coenzyme Q
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,768,00.html

Coenzyme Q10
Source: Integrative Medicine Communications; www.drkoop.com

Coq10
Source: Integrative Medicine Communications; www.drkoop.com

Dehydroepiandrosterone (DHEA)
Source: Integrative Medicine Communications; www.drkoop.com

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

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

Fenugreek
Alternative names: Trigonella foenum-graecum
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

Fo-Ti
Alternative names: Polygonum multiflorum
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

Guggul
Alternative names: Commiphora mukul
Source: Healthnotes, Inc.; www.healthnotes.com

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

Gugulipid
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10033,00.html

He Shou Wu
Source: Prima Communications, Inc.www.personalhealthzone.com

Hong Qu
Source: Integrative Medicine Communications; www.drkoop.com

Hung-Chu
Source: Integrative Medicine Communications; www.drkoop.com

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

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

Kava
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,798,00.html

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

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

Milk Thistle
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10044,00.html

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

Plantago Isphagula
Source: Integrative Medicine Communications; www.drkoop.com

Psyllium
Alternative names: Plantago ovata, Plantago ispaghula
Source: Healthnotes, Inc.; www.healthnotes.com

Psyllium
Alternative names: Ispaghula,Plantago isphagula
Source: Integrative Medicine Communications; www.drkoop.com

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

Red Koji
Source: Integrative Medicine Communications; www.drkoop.com

Red Leaven
Source: Integrative Medicine Communications; www.drkoop.com

Red Rice
Source: Integrative Medicine Communications; www.drkoop.com

Red Yeast Rice
Alternative names: Monascus purpureus
Source: Healthnotes, Inc.; www.healthnotes.com

Red Yeast Rice
Alternative names: Angkak, Beni-koju, Hong Qu, Hung-chu, Monascus, Red Leaven, Red Rice, Red Koji, Zhitai, Xue Zhi Kang
Source: Integrative Medicine Communications; www.drkoop.com

Red Yeast Rice
Source: Prima Communications, Inc.www.personalhealthzone.com

Red Yeast Rice
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10054,00.html

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

St. John's Wort
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,824,00.html

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

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

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

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

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

Zingiber
Alternative names: Ginger; Zingiber officinale Roscoe
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

Zue Zhi Kang
Source: Integrative Medicine Communications; www.drkoop.com

General References

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

CHAPTER 4. PATENTS ON HYPERLIPIDEMIA

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.[8] 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 "hyperlipidemia" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on hyperlipidemia, we have not necessarily excluded non-medical patents in this bibliography.

Patents on Hyperlipidemia

By performing a patent search focusing on hyperlipidemia, 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

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[8]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 hyperlipidemia:

- **Composition and method for treatment of gastrointestinal disorders and hyperlipidemia**

  Inventor(s): Bojrab; Gregory G. (Indianapolis, IN)

  Assignee(s): Lacpro Industries, Inc. (Indianapolis, IN)

  Patent Number: 6,696,057

  Date filed: July 31, 2000

  Abstract: A probiotic composition and method for the treatment of gastrointestinal disorders, **hyperlipidemia** and autoimmune diseases. The probiotic composition comprises a culture having lactobacillus bulgaricus and streptococcus thermophilus lactic acid bacteria and a carbohydrate enriched media, whereby the culture and media are combined and allowed to ferment until a desired ratio of the lactobacillus bulgaricus and streptococcus thermophilus organisms as well as a desired number of total organisms per dose are achieved. The method of the present invention comprises the steps of providing a probiotic composition of the present invention and administering the composition to a patient having at least one of gastrointestinal disorders, **hyperlipidemia** or autoimmune diseases.

  Excerpt(s): The present invention relates to the field of treatment of gastrointestinal disorders, **hyperlipidemia** and autoimmune diseases. More particularly, the present invention relates to a probiotic composition having lactic acid bacteria of the genius/species lactobacillus bulgaricus and streptococcus thermophilus, and a method of treatment using the same. Gastrointestinal disease includes many disorders, including but not limited to, inflammatory bowel diseases such as ulcerative colitis and Crohn's disease, infectious enteritis (viral, bacterial, parasitic), antibiotic associative diarrhea, clostridium difficile colitis, microscopic or lymphocytic colitis, collagenous colitis, colon polyps and familial polyp syndromes (e.g., familial polyposis syndrome, Gardner's Syndrome), helicobacter pylori, irritable bowel syndrome, nonspecific diarrheal illnesses, and intestinal cancers. The cause of many of these diseases is unknown. Such is the case with inflammatory bowel disease ("IBD"), the general term for diseases that cause inflammation in the intestines. For example, ulcerative colitis ("UC") is an IBD that causes inflammation of the mucosa lining of the large intestine. The inflammation usually occurs in the rectum and lower part of the colon, but it may affect the entire colon.

  Web site: http://www.delphion.com/details?pn=US06696057__

- **Genes expressed in treated human C3A liver cell cultures**

  Inventor(s): Kaser; Matthew R. (Castro Valley, CA)

  Assignee(s): Incyte Corporation (Palo Alto, CA)

  Patent Number: 6,727,066

  Date filed: July 30, 2001

  Abstract: The present invention relates to a composition comprising a plurality of cDNAs which are differentially expressed in treated human C3A liver cell cultures and

which may be used entirely or in part to diagnose, to stage, to treat, or to monitor the progression or treatment of liver disorders such as **hyperlipidemia.**

Excerpt(s): 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 disease. For example, both the levels and sequences expressed in tissues from subjects with **hyperlipidemia** may be compared with the levels and sequences expressed in normal tissue.

Web site: http://www.delphion.com/details?pn=US06727066__

- **Hypoglycemic sulfonyl pyrazolones and pyrazolines**

  Inventor(s): Dominianni; Samuel James (Indianapolis, IN)

  Assignee(s): Eli Lilly and Company (Indianapolis, IN)

  Patent Number: 6,617,342

  Date filed: April 16, 2002

  Abstract: This invention provides compounds and their pharmaceutically acceptable salts, pharmaceutical formulation of said compounds and methods for treating hyperglycemia associated with non-insulin dependant diabetes and for treating **hyperlipidemia.**

  Excerpt(s): This invention relates to the treatment and control of hyperglycemia, such as occurs in non-insulin-dependent diabetes mellitus (NIDDM). This invention also relates to treatment and control of **hyperlipidemia.** The disease, diabetes mellitus, is recognized in two forms. Type I diabetes requires exogenous insulin for control of the disease because it appears that endogenous production of insulin by the Isles of Langerhans in the pancreas is extremely poor or non-existent. Type I diabetes is often referred to as insulin-dependent diabetes mellitus (IDDM). Type II, non-insulin-dependent diabetes mellitus (NIDDM), is characterized by defects of insulin sensitivity in peripheral tissues such as adipose tissue and muscle, as described by J. E. Gerich in New Engl. J. Med., 321, 1231-1245 (1989). Hyperlipidemia is often observed in diabetics (Diabetes Care, 18, Supplement 1, 86-93, 1995). The combination of **hyperlipidemia** and hyperglycemia greatly increases the risk of cardiovascular diseases in diabetics. Successful treatment of **hyperlipidemia** and hyperglycemia in diabetics is needed urgently.

  Web site: http://www.delphion.com/details?pn=US06617342__

- **Hypolipidemic and antioxidant morpholine derivatives**

  Inventor(s): Chrysselis; Michael (Thessaloniki, GR), Kourounakis; Panagiotis (Thessaloniki, GR), Rekka; Eleni (Thessaloniki, GR)

  Assignee(s): Elpen S.A. (Pikermi Attica, GR)

  Patent Number: 6,693,192

  Date filed: October 11, 2001

  Abstract: The present invention relates to the synthesis and the evaluation of the antioxidant, hypocholesterolemic and hypolipidemic activity of substituted morpholine derivatives of formula (I) in which R.sub.1 =CH.sub.2 CH.sub.3, R.sub.2 =CH.sub.3, R.sub.3, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 1) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.2 ONO.sub.2, R.sub.2 =CH.sub.3, R.sub.3, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 2) or R.sub.1 =H, R.sub.2 --R.sub.3 =(CH.sub.2).sub.4, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 3) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.3, R.sub.2 --R.sub.3 =(CH.sub.2)4, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 4) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.2 ONO.sub.2, R.sub.2 --R.sub.3 =(CH.sub.2).sub.4, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 5) or R.sub.1 =H, R.sub.2 =CH.sub.3, R.sub.3 --R.sub.4 =(CH.sub.2).sub.4, R.sub.5 =C.sub.6 H.sub.5 (compound 6) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.3, R.sub.2 =CH.sub.3, R.sub.3 --R.sub.4 =(CH.sub.2).sub.4, R.sub.5 =C.sub.6 H.sub.5 (compound 7) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.2 ONO.sub.2, R.sub.2 =CH.sub.3, R.sub.3 --R.sub.4 =(CH.sub.2).sub.4, R.sub.5 =C.sub.6 H.sub.5 (compound 8) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.2 ONO.sub.2, R.sub.2 =CH.sub.3, R.sub.3, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 9) or R.sub.1 =H, R.sub.2 =p-NO.sub.2 --C.sub.6 H.sub.4 --CH.sub.2 CH.sub.2, R.sub.3, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 10). The 2-hydroxy-morpholine derivatives 3, 6 and 10 are synthesised by the reaction of the appropriate aminoalcohol (22 mmol) and the 2-bromophenylacetophenone or the 2-bromoacetophenone (10 mmol) in ether and acetone for 15 hours at room temperature. Me 2-alkoxy derivatives 1, 4 and 7 are synthesised by the reaction of the respective 2-hydroxy derivative with the appropriate alcohol, in acid medium and reflux. Compounds 2, 5, 8 and 9 are synthesised by the reaction of the respective 2-hydroxy derivative with the 3-bromopropanol in acidic medium and reflux. The 2-(3-bromopropoxy) derivatives thin reacted with silver nitrate in acetonitrile and reflux. The compounds of formula (I) decrease significantly total cholesterol, triglyceride and LDL-cholesterol levels in plasma. The compounds of formula (I) possess potent antioxidant activity. The compounds of formula (I) with the above properties could be useful to the treatment of hypercholesterolemia, **hyperlipidemia** and atheromatosis.

  Excerpt(s): in which R.sub.1 =CH.sub.2 CH.sub.3, R.sub.2 =CH.sub.3, R.sub.3, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 1) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.2 ONO.sub.2, R.sub.2 =CH.sub.3, R.sub.3, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 2) or R.sub.1 =H, R.sub.2 13 R.sub.3 =(CH.sub.2).sub.4, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 3) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.3, R.sub.2 --R.sub.3 =(CH.sub.2).sub.4, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 4) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.2 ONO.sub.2 R.sub.2 --R.sub.3 =(CH.sub.2).sub.4, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 5) or R.sub.1 =H, R.sub.2 =CH.sub.3, R.sub.3 --R.sub.4 =(CH.sub.2).sub.4, R.sub.5 =C.sub.6 H.sub.5 (compound 6) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.3, R.sub.2 =CH.sub.3, R.sub.3 --R.sub.4 =(CH.sub.2).sub.4, R.sub.5 =C.sub.6 H.sub.5 (compound 7) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.2 ONO.sub.2, R.sub.2 =CH.sub.3, R.sub.3 --R.sub.4 =(CH.sub.2)4, R.sub.5 =C.sub.6 H.sub.5 (compound 8) or R.sub.1 =CH.sub.2 CH.sub.2 CH.sub.2 ONO.sub.2, R.sub.2

=CH.sub.3, R.sub.3, R.sub.4 =H, R.sub.5 =H (compound 9) or R.sub.1 =H, R.sub.2 =p-NO.sub.2 --C.sub.6 H.sub.4 --CH.sub.2 CH.sub.2, R.sub.3, R.sub.4 =H, R.sub.5 =C.sub.6 H.sub.5 (compound 10). thrombogenesis, endothelial injury and haemodynamic factors. Especially, the oxidative modification of LDL appears to be the most risk atherogenic process, which induces inflammatory and apoptotic mechanisms and finally the formation of foam cells and fatty streaks.

Web site: http://www.delphion.com/details?pn=US06693192__

- **Intermediate release nicotinic acid compositions for treating hyperlipidemia having unique biopharmaceutical characteristics**

  Inventor(s): Cefali; Eugenio A. (Lauderhill, FL)

  Assignee(s): Kos Pharmaceuticals, Inc. (Miami, FL)

  Patent Number: 6,746,691

  Date filed: October 31, 1997

  Abstract: Intermediate release nicotinic acid formulations having unique biopharmaceutical characteristics, which are suitable for oral administration once per day as a single dose preferably administered during the evening or at night for treating **hyperlipidemia** without causing drug-induced hepatotoxicity to such a level that requires the therapy to be discontinued, are disclosed. The intermediate nicotinic acid formulations can be administered as tablets in dosage strengths of, for example, 375 mg, 500 mg, 750 mg and 1000 mg. The 375 mg, 500 mg and 750 mg nicotinic acid tablets of the present invention have a dissolution curve similarity fit factor F.sub.2 of at least about 79, and the 1000 mg nicotinic acid tablets of the present invention have a dissolution curve similarity fit factor F.sub.2 of at least 44.

  Excerpt(s): The present invention is directed to intermediate release nicotinic acid formulations having unique biopharmaceutical characteristics, which are useful for treating **hyperlipidemia** and methods of treating **hyperlipidemia** employing such compositions. Another aspect of the present invention, the nicotinic acid formulations are suitable for once a day dosing without causing drug-induced hepatotoxicity to a level which would require the therapy to be discontinued. More particularly, the present invention employs a composition of nicotinic acid, derivatives and mixtures thereof, and a swelling agent to form an intermediate timed-release sustaining composition for nocturnal or evening dosing. Specifically, the present invention employs a composition of nicotinic acid and hydroxypropyl methylcellulose to treat **hyperlipidemia** in a once per day oral dosage form given during the evening hours that causes little if any hepatotoxicity. Nicotinic acid, 3-pyridinecarboxylic acid or niacin, is an antilipidemic agent that is marketed under, for example, the trade names Nicolar.RTM., SloNiacin.RTM., Nicobid.RTM. and Time Release Niacin.RTM. Nicotinic acid has been used for many years in the treatment of lipidemic disorders such as **hyperlipidemia,** hypercholesterolemia and atherosclerosis. This compound has long been known to exhibit the beneficial effects of reducing total cholesterol, low density lipoproteins or "LDL cholesterol," triglycerides and apolipoprotein a (Lp(a)) in the human body, while increasing desirable high density lipoproteins or "HDL cholesterol". The dosing regimen of IR nicotinic acid is known to provide a very beneficial effect on blood lipids as discussed in Knopp et al.; "Contrasting Effects of Unmodified and Time-Release Forms of Niacin on Lipoproteins in Hyperlipidemic Subjects: Clues to Mechanism of Action of Niacin"; Metabolism 34/7, 1985, page 647. The chief advantage of this profile is the ability of IR nicotinic acid to decrease total cholesterol, LDL cholesterol, triglycerides

and Lp(a) while increasing HDL particles. In fact, IR nicotinic acid has been well regarded as an effective drug in the treatment of **high cholesterol** since about the early 1960s. Unfortunately, IR nicotinic acid has never really become widely used because of the high incidence of flush that often occurs when an IR dose is taken. That means an individual may develop a visible, uncomfortable, hot or flushed feeling three or four times a day for about one hour following each IR dose.

Web site: http://www.delphion.com/details?pn=US06746691__

- **Method for treating hypercholesterolemia, hyperlipidemia, and atherosclerosis**

  Inventor(s): Cherukuri; Reddy Sastry V. (Folsom, CA), Cheruvanky; Rukmini (Folsom, CA), Lynch; Ike (El Dorado Hills, CA), McPeak; Patricia (El Dorado Hills, CA), Qureshi; Asaf A. (Madison, WI)

  Assignee(s): The RiceX Company (El Dorado Hills, CA)

  Patent Number: 6,733,799

  Date filed: May 5, 2003

  Abstract: A method for reducing mammalian serum total cholesterol, LDL cholesterol, apolipoprotein B and triglyceride levels, by ingesting a stabilized rice bran derivative selected from the group consisting of an enzyme treated stabilized rice bran, an insolubilized fraction and mixtures thereof, thereby reducing serum total cholesterol, LDL cholesterol, apolipoprotein B and triglyceride levels in said mammal.

  Excerpt(s): The present invention relates to methods for treating hypercholesterolemia, **hyperlipidemia,** and atherosclerosis in mammals by ingesting a stabilized rice bran derivative. Hypercholesterolemia is a condition with elevated levels of circulating total cholesterol, LDL-cholesterol and VLDL-cholesterol as per the guidelines of the Expert Panel Report of the National Cholesterol Educational Program (NCEP) of Detection, Evaluation of Treatment of **high cholesterol** in adults (see, Arch. Int. Med. (1988) 148, 36-39). In particular, high level of LDL and VLDL are positively associated with coronary arteriosclerosis while the high levels of high density lipoproteins (HDL) are negative risk factors. The role of LDL oxidation is gaining much attention in the literature. It is well documented that LDL becomes oxidatively stressed under pathological conditions and is no longer recognized by the LDL receptors. The oxidized LDL is taken up by macrophages within the subendothelial space, leading to the formation of fatty streaks which are the basis of most advanced lesions. Hypercholesterolemia is implicated as a high risk factor of cardiovascular disease (CVD), including arteriosclerosis, atherosclerosis and xanthomatosis in humans. Hypercholesterolemia is influenced by diet, heredity, environment, life style, diseases and stress, leading to heart attacks and strokes at an early age.

  Web site: http://www.delphion.com/details?pn=US06733799__

- **Methods and compositions employing red rice fermentation products**

  Inventor(s): Peng; Chi-Xiu (Beijing, CN), Zhang; Mao Liang (Beijing, CN), Zhou; Yu-Fang (Beijing, CN)

  Assignee(s): Peking University (Bejing, CN)

  Patent Number: 6,632,428

  Date filed: April 4, 2000

  Abstract: Methods and compositions are disclosed which comprise red rice fermentation products, that can be used as natural dietary supplements and/or medicaments for the treatment or prevention of **hyperlipidemia** and associated disorders and symptoms, such as cardiovascular diseases, cerebrovascular diseases, diabetes, hypertension, obesity, asthenic breathing, chronic headache, chest pain and tightness, limb swelling and distention, loss of appetite and excess expectoration. The methods and compositions are effective in lowering both the serum cholesterol and serum triglyceride levels in humans, and can be used for maintaining cardiovascular health. The invention also encompasses particular Monascus strains that yield fermentation products with the desired biological activities.

  Excerpt(s): The invention relates to the fields of rice fermentation and treatment of **hyperlipidemia.** More particularly, the invention relates to red rice fermentation products and methods, and use of the products to treat **high cholesterol** levels and other disorders. The invention relates to compositions comprising red rice fermentation products, that can be used as dietary supplements and/or therapeutic medicaments. For example, the compositions can be used to lower serum cholesterol and triglycerides in mammals. Further, the invention relates to methods of treating cardiovascular disorders and other diseases using the red rice fermentation products. In addition, the invention relates to particular Monascus strains that yield fermentation products with the desired biological activities. Red rice is known mostly for its use in food as a preservative and colorant, and its uses in the dye industry. Red rice (known in Chinese as Hung-ch'u or Hongqu) has also been known and used for hundreds of years in China in rice wine making and as a food preservative. In addition, red rice has been known as an ancient Chinese medicine or an ingredient in certain ancient Chinese prescriptions.

  Web site: http://www.delphion.com/details?pn=US06632428__

- **Process for the preparation of amorphous atorvastatin calcium**

  Inventor(s): Balazs; Laszlo (Budapest, HU), Barkoczy; Jozsef (Budapest, HU), Barta; Ferenc (Tiszavasvari, HU), Doman; Imre (Budapest, HU), Donath; Gyorgyi Vereczkeyne (Budapest, HU), Greff; Zoltan (Budapest, HU), Kirallyi; Zsuzsa Szent (Budapest, HU), Nagy; Kalman (Budapest, HU), Nagy; Peter Kotay (Vac, HU), Ratkai; Zoltan (Budapest, HU), Seres; Peter (Budapest, HU), Simig; Gyula (Budapest, HU)

  Assignee(s): Egis Gyogyszergyar Rt. (Budapest, HU)

  Patent Number: 6,646,133

  Date filed: July 3, 2002

  Abstract: The invention relates to a process for the preparation of amorphous atorvastatin calcium by recrystallization of crude atorvastatin from an organic solvent which comprises dissolving crude amorphous atorvastatin calcium in a lower alkanol containing 2-4 carbon atoms or a mixture of such alkanols under heating and isolating

the amorphous atorvastatin calcium precipitated after cooling. The atorvastatin calcium obtained is a known valuable agent useful in treating **hyperlipidemia** and hypercholestrolemia.

Excerpt(s): The invention relates to an improved new process for the preparation of atorvastatin calcium. The calcium salt of [R-(R.sup.x,R.sup. x)]-2-(4-fluorophenyl)-.beta.,.delta.-dihydroxy-5-[1-methyl-ethyl)-3-pheny l-4-[(phenylamino)-carbonyl]-1H-pyrrole-1-heptanoic acid having the INN atorvastatin is an inhibitor of the 3-hydroxy-3-methylglutamine coenzyme A reductase enzyme. Due to this effect atorvastatin is a valuable lipide and cholesterol level decreasing agent and useful in treating **hyperlipidemia** and hypercholesterolemia. Atorvastatin was described the first time in U.S. Pat. No. 5,273,995. In this US patent specification there is no disclosure concerning the crystalline form of the product. The preparation of atorvastatin and key intermediates useful in the synthesis are described at several places in prior art (e.g. U.S. Pat. No. 5,003,080, U.S. Pat. No. 5,097,045, U.S. Pat. No. 5,103,024, U.S. Pat. No. 5,124,482, U.S. Pat. No. 5,149,837, U.S. Pat. No. 5,155,251, U.S. Pat. No. 5,216,174, U.S. Pat. No. 5,245,047, U.S. Pat. No. 5,248,793, U.S. Pat. No. 5,280,126, U.S. Pat. No. 5,397,792 and U.S. Pat. No. 5,342,952). The preparation of atorvastatin calcium in a defined crystalline form is first described in WO 97/03958.

Web site: http://www.delphion.com/details?pn=US06646133__

- **Processes for the preparation of tricyclic amino alcohol derivatives**

  Inventor(s): Ishii; Naoyuki (Nobeoka, JP), Matsubara; Koki (Fuji, JP), Ogawa; Masami (Fuji, JP)

  Assignee(s): Asahi Kasei Kabushiki Kaisha (Osaka, JP)

  Patent Number: 6,696,573

  Date filed: March 4, 2002

  Abstract: A process for the preparation of tricyclic amino alcohol derivatives including 2-[N-[2-(9H-carbazol-2-yloxy)ethyl]]amino-1-[(3-methylsulfonylamino)phenyl]ethanol useful in the treatment of diabetes, obesity, **hyperlipidemia** and so on; and intermediates as represented by formula (5) or (6) or the like useful in the preparation, wherein R11 is hydrogen or the like; and *1 represents an asymmetric carbon atom. 2-Halo-1-(3-nitrophenyl)ethanone derivatives and 1-(3-nitrophenyl)oxirane derivatives, which are intermediates for the preparation of tricyclic amino alcohol derivatives, are easy of purification, and particularly optically active 1-(3-nitrophenyl)oxirane derivatives are effective in enhancing the optical purities of the final products.

  Excerpt(s): wherein X represents NH, O or S, R.sup.5 represents a hydrogen atom or a hydroxyl, amino or acetylamino group, and *2 represents an asymmetric carbon atom when R.sup.5 is not a hydrogen atom, or salts thereof, which are useful in the treatment and prevention of diabetes, obesity, **hyperlipidemia** and the like; and intermediates useful for the process. However, the study on the above known processes carried out by the present inventors has shown that these processes are not necessarily practical. There would be a need for a more convenient, practical preparation process with low cost which comprises a small number of steps with good industrial efficiency. This chiral auxiliary agent is very expensive and the process for the preparation thereof is very complicated. The chiral auxiliary agent is a hazardous, combustible substance and an asymmetric reduction using the said chiral auxiliary agent requires strictly anhydrous

conditions, strict temperature controls, complicated works and the like, which will become problematic when the chiral auxiliary agent is industrially used.

Web site: http://www.delphion.com/details?pn=US06696573__

- **Regulators of PPAR.delta. (.beta.) and their use in the treatment of obesity and insulin resistance**

  Inventor(s): Hariharan; Narayanan (Richboro, PA)

  Assignee(s): Bristol-Myers Squibb Company (Princeton, NJ)

  Patent Number: 6,677,298

  Date filed: July 19, 2001

  Excerpt(s): The present invention relates to a method for treating obesity, insulin resistance and dyslipidemia in mammals including humans through inhibition of PPAR.delta.(.beta.). This invention also relates to methods of screening for chemical entities that act to regulate PPAR.delta.(.beta.) activity. The invention further relates to a method of treatment of obese, insulin resistant and hyperlipidemic patients with one or more combinations of a PPAR.delta.(.beta.) antagonist, an anti-diabetic agent and a lipid-lowering agent. Obesity is a common clinical problem in most developed nations and is also rapidly becoming a major health concern in developing nations. Overweight individuals frequently suffer from several metabolic disorders such as insulin resistance, type 2 diabetes and dyslipidemia. These individuals also frequently suffer from hypertension, increased risk for cardiovascular diseases such as atherosclerosis and coronary heart disease, and osteoarthritis of the joints. In mammals, including humans, adipocytes (fat cells) store excess energy in the form of triglycerides at times of nutritional excess (see Lowell, Cell, 99:239-242, 1999). During starvation, triglycerides are degraded to fatty acids in adipocytes in order to supplement nutritional and energy requirements. However, excess adiposity achieved either through recruitment of progenitor cells (pre-adipocytes) to become adipocytes (differentiation) and/or through expansion of the pre-existing adipocytes (hypertrophy), is associated with obesity (see Lowell, Cell, 99:239-242, 1999). Hypertrophied adipocytes have been demonstrated to produce excessive amounts of cytokines such as TNF.alpha.(which in turn act to reduce insulin receptor activity and/or response to insulin signaling in skeletal muscle and adipocytes, two major glucose utilizing tissues (see Hotamisligil, et al., Science, 259:87-90, 1993; Lowell, Cell, 99:239-242, 1999). This results in insulin resistance, reduced glucose uptake, and in some individuals type 2 diabetes. Obese individuals with insulin resistance and type 2 diabetes also frequently suffer from **hyperlipidemia,** atherosclerosis and cardiovascular diseases (see Rosenbaum et al., New. Eng. J. Med. 337:396-407, 1997).

  Web site: http://www.delphion.com/details?pn=US06677298__

- **Topical formulations for the transdermal delivery of niacin and methods of treating hyperlipidemia**

  Inventor(s): Jacobson; Elaine L. (Tucson, AZ), Jacobson; Myron K. (Tucson, AZ), Kim; Hyuntae (Tucson, AZ), Kim; Moonsun (Tucson, AZ), Qasem; Jaber G. (Tucson, AZ)

  Assignee(s): University of Kentucky Research Foundation (Lexington, KY)

  Patent Number: 6,677,361

  Date filed: April 16, 2001

  Abstract: Niacin and niacin prodrugs are topically administered as suitable formulations to device for impoving the lipid profiles of subjects, preferably humans.

  Excerpt(s): This invention relates to topical formulations for transdermal delivery of niacin and esters and alcoholic fatty-acid esters as described herein derivatives thereof and the transdermal treatment of **hyperlipidemia** and hypercholesterolemia with these agents. Therapeutic uses of the system are also described. The topical formulations are useful for, e.g., treating **hyperlipidemia** in a mammal. Hyperlipidemia and hypercholesterolemia are conditions that have a well established correlation with increased risk of other conditions, such as heart attacks, atherosclerosis, and other deleterious ailments. There are numerous agents available for lowering cholesterol and lipid levels, including gemfibrizol, probucol, and, more recently, the "statins" e.g, lovastatin. Niacin (nicotinic acid), a water soluble B-complex vitamin, is used orally for the treatment of **hyperlipidemia** and has been shown to be effective in reducing total plasma cholesterol (C), low density lipoproteins LDL-C and very low density lipoprotein triglycerides (VLDL-triglycerides), all of which are associated with health risks, while raising serum levels of high density lipoproteins (HDL-C) which are considered a "healthy" lipoprotein, in patients with type II, III, IV, and V hyperlipoproteinemia.

  Web site: http://www.delphion.com/details?pn=US06677361__

- **Use of (-) (3-trihalomethylphenoxy) (4-halophenyl) acetic acid derivatives for treatment of insulin resistance, type 2 diabetes, hyperlipidemia and hyperuricemia**

  Inventor(s): Luo; Jian (Brisbane, CA), Luskey; Kenneth L. (Saratoga, CA)

  Assignee(s): DiaTex, Inc. (San Antonio, TX), Metabolex, Inc. (Hayward, CA)

  Patent Number: 6,613,802

  Date filed: June 2, 2000

  Abstract: The present invention provides the use of (-) (3-trihalomethylphenoxy) (4-halophenyl) acetic acid derivatives and compositions in the treatment of insulin resistance, Type 2 diabetes, **hyperlipidemia** and hyperuricemia.

  Excerpt(s): The present invention relates to the use of (-) (3-trihalomethylphenoxy) (4-halophenyl) acetic acid derivatives and compositions in the treatment of insulin resistance, Type 2 diabetes, **hyperlipidemia** and hyperuricemia. Diabetes mellitus, commonly called diabetes, refers to a disease process derived from multiple causative factors and characterized by elevated levels of plasma glucose, referred to as hyperglycemia. See, e.g., LeRoith, D. et al., (eds.), DIABETES MELLITUS (Lippincott-Raven Publishers, Philadelphia, Pa. U.S.A. 1996), and all references cited therein. According to the American Diabetes Association, diabetes mellitus is estimated to affect approximately 6% of the world population. Uncontrolled hyperglycemia is associated

with increased and premature mortality due to an increased risk for microvascular and macrovascular diseases, including nephropathy, neuropathy, retinopathy, hypertension, cerebrovascular disease and coronary heart disease. Therefore, control of glucose homeostasis is a critically important approach for the treatment of diabetes. There are two major forms of diabetes: Type 1 diabetes (formerly referred to as insulin-dependent diabetes or IDDM); and Type 2 diabetes (formerly referred to as non-insulin dependent diabetes or NIDDM).

Web site: http://www.delphion.com/details?pn=US06613802__

Patent Applications on Hyperlipidemia

As of December 2000, U.S. patent applications are open to public viewing.[9] 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 hyperlipidemia:

- **Bioavailable fenofibrate compositions, methods for treating hyperlipidemia and hypercholesterolemia and processes for the preparation of such compositions**

  Inventor(s): Femia, Robert A.; (Kinnelon, NJ), Fishkis, Oscar I.; (White Plains, NY), Patel, Damodar P.; (Elmwood Park, NJ), Ragunathan, Narayan; (West Nyack, NY)

  Correspondence: The Firm OF Karl F Ross; 5676 Riverdale Avenue; PO Box 900; Riverdale (bronx); NY; 10471-0900; US

  Patent Application Number: 20040142903

  Date filed: January 16, 2003

  Abstract: Pharmaceutical compositions for treating **hyperlipidemia** or hypercholesterolemia in mammals are described which comprise: 1 (a) fenofibrate 5 to 35 wt. -% (b) a cyclodextrin 4 to 30 wt. -% (c) an alkali metal or 0.1 to 10 wt. -%; and alkaline earth metal docusate and/or alkali metal or alkaline earth metal lauryl sulfate (d) a water-insoluble, wettable 5 to 30 wt. -% inorganic carrier capable of forming a dispersion of the fenofibrate and a pharmaceutically acceptable inert carrier or diluent.A therapeutically effective amount of the compositions are orally administered to mammals to treat **hyperlipidemia** or hypercholesterolemia.

  Excerpt(s): This invention relates to novel fenofibrate compositions with bioavailability. The invention further relates to compositions containing fenofibrate, a cyclodextrin, an alkaline metal or alkaline earth metal docusate and/or an alkali metal or alkaline earth metal lauryl sulfate, and a water-insoluble, wettable carrier which provide fenofibrate to patients in a highly bioavailable form without the need for co-micronization of fenofibrate with any of the other ingredients. Fenofibrate is a well known antihyperlipoproteinemic agent. See U.S. Pat. No. 4,058,552. Experience with oral administration of fenofibrate has shown that the bioavailability of the drug has not been as high as would be desirable. A good deal of research has been carried out over the years to obtain compositions containing fenofibrate that are orally administered to patients and which have improved bioavailability. According to U.S. Pat. No. 4,895,726 to CURTET et al compositions containing fenofibrate with improved bioavailability have been prepared in which the fenofibrate has been co-micronized in an intimate

[9] This has been a common practice outside the United States prior to December 2000.

mixture with a solid surfactant such as sodium lauryl sulfate. CURTET et al expressly state that it is possible to improve the bioavailability to a significantly greater extent than that which would be achieved either by adding a surfactant, or by micronizing the fenofibrate on its own, or by intimately mixing the separately micronized fenofibrate and surfactant. Such a fenofibrate-containing composition is currently available on the market under the mark TRICOR.sup.R. Among the compositions actually exemplified in CURTET et al, all such compositions contain alpha-lactose monohydrate, a well known hydrosoluble carrier. The alpha-lactose monohydrate is added to the co-micronizate of fenofibrate and solid surfactant.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Biphenylcarboxamides useful as lipid lowering agents**

  Inventor(s): Backx, Leo Jacobs Jozef; (Beerse, BE), Meerpoel, Lieven; (Beerse, BE)

  Correspondence: Philip S. Johnson; Johnson & Johnson; One Johnson & Johnson Plaza; New Brunswick; NJ; 08933-7003; US

  Patent Application Number: 20040102490

  Date filed: December 24, 2003

  Abstract: Biphenylcarboxamide compounds of formula (I) 1methods for preparing such compounds, pharmaceutical compositions comprising said compounds as well as the use of said compounds as a medicine for the treatment of **hyperlipidemia,** obesity and type II diabetes.

  Excerpt(s): The present invention is concerned with novel biphenylcarboxamide compounds having apolipoprotein B inhibiting activity and concomitant lipid lowering activity. The invention further relates to methods for preparing such compounds, pharmaceutical compositions comprising said compounds as well as the use of said compounds as a medicine for the treatment of **hyperlipidemia,** obesity and type II diabetes. Obesity is the cause of a myriad of serious health problems like the adult onset of diabetes and heart disease. In addition, the loss of weight is getting an obsession among an increasing proportion of the human population. The causal relationship between hypercholesterolemia, particularly that associated with increased plasma concentrations of low density lipoproteins (hereinafter referred as LDL) and very low density lipoproteins (hereinafter referred as VLDL), and premature atherosclerosis and/or cardiovascular disease is now widely recognized. However, a limited number of drugs are presently available for the treatment of **hyperlipidemia.** Drugs primarily used for the management of **hyperlipidemia** include bile acid sequestrant resins such as cholestyramine and colestipol, fibric acid derivatives such as bezafibrate, clofibrate, fenofibrate, ciprofibrate and gemfibrozil, nicotinic acid and cholesterol synthesis-inhibitors such as HMG Co-enzyme-A reductase inhibitors. The inconvenience of administration (a granular form to be dispersed in water or orange juice) and the major side-effects (gastro-intestinal discomfort and constipation) of bile acid sequestrant resins constitute major drawbacks. Fibric acid derivatives induce a moderate decrease (by 5 to 25%) of LDL cholesterol (except in hypertriglyceridemic patients in whom initially low levels tend to increase) and, although usually well tolerated, suffer from side-effects including potentiation of warfarine, pruritus, fatigue, headache, insomnia, painful reversible myopathy and stiffness in large muscle groups, impotency and impaired renal function. Nicotinic acid is a potent lipid lowering agent resulting in a 15 to 40% decrease in LDL cholesterol (and even 45 to 60% when combined with a bile acid sequestrant resin) but with a high incidence of troublesome side-effects related to the

drug's associated vasodilatory action, such as headache, flushing, palpitations, tachychardia and occasional syncopes, as well as other side-effects such as gastro-intestinal discomfort, hyperucemia and impairment of glucose tolerance. Among the family of HMG Co-enzyme-A reductase inhibitors, lovastatin and simvastatin are both inactive prodrugs containing a lactone ring which is hydrolyzed in the liver to form the corresponding active hydroxy-acid derivative. Inducing a reduction of LDL cholesterol by 35 to 45%, they are generally well tolerated with a low incidence of minor side effects. However there still remains a need for new lipid lowering agents with improved efficiency and/or acting via other mechanisms than the above mentioned drugs.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Combinations of HMG-CoA reductase inhibitors and nicotinic acid compounds and methods for treating hypelipidemia once a day at night**

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  Patent Application Number: 20040053975

  Date filed: September 2, 2003

  Abstract: The present invention relates to solid pharmaceutical combinations for oral administration comprising nicotinic acid or a nicotinic acid compound or mixtures thereof in an extended release form and an HMG-CoA reductase inhibitor, which are useful for altering lipid levels in subjects suffering from, for example, **hyperlipidemia** and atherosclerosis, without causing drug-induced hepatotoxicity, myopathy or rhabdomyolysis. The present invention also relates to methods of altering serum lipids in subjects to treat, for example, **hyperlipidemia** in hyperlipidemics, lipidemia in normolipidemics diagnosed with or predisposed to cardiovascular disease, and atherosclerosis, by administering such oral solid pharmaceutical combinations once per day as a single dose during the evening hours, without causing drug-induced hepatotoxicity, myopathy or rhabdomyolysis, or without causing in at least an appreciable number of individuals drug-induced hepatotoxicity, myopathy or rhabdomyolysis to such a level that discontinuation of such therapy would be required. More particularly, the present invention concerns oral solid pharmaceutical combinations comprised of, for example, (1) an HMG-CoA reductase inhibitor for immediate or extended release, (2) nicotinic acid, a nicotinic acid compound or mixtures thereof and (3) a swelling agent to form a sustained release composition for extended release of the nicotinic acid or nicotinic acid compound or mixtures thereof for nocturnal or evening dosing for reducing serum lipids and increasing HDL-cholesterol. In accordance with the present invention, and by way of example, a composition for oral administration during the evening hours to alter serum lipids comprised of nicotinic acid and hydroxypropyl methylcellulose in the form of an extended or sustained release tablet or caplet coated with a coating comprising an HMG-CoA reductase inhibitor in immediate release form is disclosed. Also in accordance with the present invention, the pharmaceutical combinations may include a nonsteroidal anti-inflammatory agent for reducing the capacity of nicotinic acid or nicotinic acid compounds to provoke flushing reactions in individuals.

  Excerpt(s): This invention generally relates to pharmaceutical combinations for oral administration comprising nicotinic acid or a nicotinic acid compound or mixtures thereof in an extended release form and 3-hydroxy-3-methylglutaryl co-enzyme A

(HMG-CoA) reductase inhibitor in an immediate or extended release form, which are useful for altering serum lipid levels in subjects when given once per day as a single dose during the evening hours, without causing drug-induced hepatotoxicity, myopathy or rhabdomyolysis. The present invention also relates to methods of orally dosing subjects with such pharmaceutical combinations once per day as a single dose during the evening hours for altering their serum lipid levels to treat, for example, **hyperlipidemia** and atherosclerosis, without causing drug-induced hepatotoxicity, myopathy or rhabdomyolysis. Hyperlipidemia or an elevation in serum lipids is associated with an increase incidence of cardiovascular disease and atherosclerosis. Specific forms of **hyperlipidemia** include, for example, hypercholesteremia, familial dysbetalipoproteinemia, diabetic dyslipidemia, nephrotic dyslipidemia and familial combined **hyperlipidemia.** Hypercholesteremia is characterized by an elevation in serum low density lipoprotein-cholesterol and serum total cholesterol. Low density lipoprotein (LDL-cholesterol) transports cholesterol in the blood. Familial dysbetalipoproteinemia, also known as Type III **hyperlipidemia,** is characterized by an accumulation of very low density lipoprotein-cholesterol (VLDL-cholesterol) particles called beta-VLDLs in the serum. Also associated with this condition, there is a replacement of normal apolipoprotein E3 with abnormal isoform apolipoprotein E2. Diabetic dyslipidemia is characterized by multiple lipoprotein abnormalities, such as an overproduction of VLDL-cholesterol, abnormal VLDL triglyceride lipolysis, reduced LDL-cholesterol receptor activity and, on occasion, Type III **hyperlipidemia.** Nephrotic dyslipidemia is difficult to treat and frequently includes hypercholesteremia and hypertriglyceridemia. Familial combined **hyperlipidemia** is characterized by multiple phenotypes of **hyperlipidemia,** i.e., Type IIa, IIb, IV, V or hyperapobetalipoproteinemia. It is well known that the likelihood of cardiovascular disease can be decree if the serum lipids, and in particular LDL-cholesterol, can be reduced. It is also well known that the progression of atherosclerosis can be retarded or the regression of atherosclerosis can be induced if serum lipids can be lowered. In such cases, individuals diagnosed with **hyperlipidemia** or hypercholesteremia should consider lipid-lowering therapy to retard the progression or induce the regression of atherosclerosis for purposes of reducing their risk of cardiovascular disease, and in particular coronary artery disease.

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- **Compositions and methods for the treatment of HIV-associated fat maldistribution and hyperlipidemia**

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  Patent Application Number: 20040106591

  Date filed: October 31, 2003

  Abstract: Compositions for treating or preventing fat maldistribution or **hyperlipidemia** resulting from anti-retroviral treatment of HIV-1 infection are disclosed. The compositions contain a conjugated fatty acid or alcohol and at least one member selected from the group consisting of a thiol-containing compound and a bioavailable form of trivalent chromium. Methods of treating a subject suffering from HIV-associated fat maldistribution or **hyperlipidemia** by administering a composition that includes a conjugated fatty acid or conjugated fatty alcohol and at least one member selected from

the group consisting of a thiol-containing compound and a bioavailable form of trivalent chromium are similarly provided.

Excerpt(s): This application claims priority to U.S. Provisional Patent Application Serial No. 60/428,246, filed Nov. 22, 2002, the entirety of which is incorporated herein by reference. The present invention relates generally to nutritional or pharmaceutical compositions and methods of use for the treatment of HIV-associated fat maldistribution and **hyperlipidemia.** As in the case with many other infections, HIV infection is accompanied by disturbances in lipid and glucose metabolism. These metabolic abnormalities are further confounded by hypercholesterolemia and hypertriglyceridemia induced by anti-retroviral (AR) drugs. It has been estimated that almost two-thirds of HIV/AIDS patients exhibit abnormal fat distribution coincident with AR-therapy (ART). Clinicians have termed this abnormal fat distribution lipodystrophy or fat maldistribution. Although various terms have been used, the term both lipodystrophy and fat maldistribution will be used here interchangeably to describe the syndrome of body shape changes related to changes in fat distribution in people with HIV/AIDS receiving AR-therapy (HIV/ART).

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- **Halogenobenzyl aminopropionic acid derivatives**

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  Patent Application Number: 20040102439

  Date filed: September 29, 2003

  Abstract: A halogenobenzylaminopropionic acid derivative represented by the following formula (1): 1or a pharmaceutically acceptable salt of the derivative, and a drug containing the same as an active ingredient for treating diabetes, **hyperlipidemia,** or similar pathological conditions.

  Excerpt(s): The present invention relates to a halogenobenzylaminopropionic acid derivative which is useful as a preventive or therapeutic agent for diabetes and **hyperlipidemia,** and to a drug containing the derivative as an active ingredient. In recent years, there have been a growing number of patients suffering from lifestyle-related diseases, especially such as diabetes and **hyperlipidemia,** as the eating habit of Japanese people is increasingly Westernized and they have less tendency to take exercise than did before. Diabetes and **hyperlipidemia** are known as critically basal diseases that could cause the development of arteriosclerosis and lead to ischemic heart diseases as a result.

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- **Hypoestoxides, derivatives and agonists thereof for use in the treatment and prophylaxis of hyperlipidemia**

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  Patent Application Number: 20040087553

  Date filed: October 28, 2003

  Abstract: Methods for treatment and prophylaxis of hyperlipidemias, including hypertriglyceridemia and hypercholesterolemia, are provided. The methods include administering to a host a therapeutically or prophylactically effective amount of a diterpene compound, such as a hypoestoxide.

  Excerpt(s): This application claims the benefit of priority under 35 U.S.C.sctn. 119 of provisional U.S. application Serial No. 60/421,533, filed Oct. 28, 2002, the contents of which are hereby incorporated by reference in their entirety, as if fully set forth. This invention relates to the use of diterpene compounds, in particular, hypoestoxides, derivatives and agonists thereof for treatment and prophylaxis of hyperlipidemias, including hypercholesterolemia and hypertriglyceridemia. Hyperlipidemias are conditions of abnormal plasma lipids, lipoproteins, and/or cholesterol levels, and include hypercholesterolemia and hypertriglyceridemia. Hyperlipidemias commonly accelerate atherosclerosis and predispose individuals to coronary heart disease. Hyperlipidemias can be inherited conditions or can be the result of a lifestyle that includes dietary excess, increased body weight and little or no vigorous exercise. (Jay H. Stein et al., Eds., Internal Medicine, 5.sup.th Ed., 1998, p. 1892.) References of interest providing background information on **hyperlipidemia** include: Foxton et al., **Hyperlipidemia,** Nursing Standard (Jun. 13, 1998) 12:49-56 and Krauss, Triglycerides and Atherogenic Lipoproteins: Rationale for Lipid Management, The American Journal of Medicine (Jul. 6, 1998) 105:58S-62S. All publications, patents, and patent documents referenced herein are incorporated by reference in their entirety as if fully set forth.

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- **Lipid metabolism and fructus crataegus**

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  Patent Application Number: 20040132816

  Date filed: January 6, 2003

  Abstract: A method for treating and/or preventing the cardiovascular and hepatic diseases induced by **hyperlipidemia** which comprises administered thereto an effective amount of bioflavonoids extract derived from fructus crataegus such as; rutin, quercetin, kaempferol and vitexin or a mixture thereof.

Excerpt(s): The present invention relates to a method for preventing and /or treating the cardiovascular and hepatic diseases induced by elevated plasma lipid level. These include **hyperlipidemia,** hypercholesterolemia, atherosclerosis, arteriosclerosis, angina pectoris, stroke (cerebro-vascular accident) and liver diseases in a mammal, the method comprises administered an effective amount of bioflavonoids extract derived from hawthorn berry (fructus crataegus) such as rutin, quercetin, kaempferol, vitexin or a mixture thereof. According to the recent studies and reports, coronary vascular diseases such as (e.g.) hyperlipidema, hypercholesterolemia, atherosclerosis, stroke (cerebro-vascular accident) have been the number one cause of deaths in the America. The study of Ross R., et al, [Nature, 362, 801-809 (1993)] confirmed that the elevated serum lipids e.g., cholesterols and triglycerides can cause deposition of fat and macrophage foam cells onto vascular endothelium and arterial walls and progressively develop into atheroma and atherosclerosis. The histo-pathological classification of the atherosclerotic lesions by Stary H. C., et al. (Circulation, 92: 1355-1374(1995)) showed that there are six types of lesions. The initial type I lesion contains only macrophages and macrophage foam cells in the vascular wall; the type II lesion contains macrophage foam cells and lipid-laden cells (fatty streak) in the smooth muscle cells. The type III lesion is atheroma, which contains lipid-laden cells (fatty streak) and scattered collections of extracellular lipid droplets and particles in the smooth muscle cells of the arterial wall. Type IV lesion contains a more disruptive core of extracellular lipid; the type V lesion contains largely calcified and some fibrous connective tissue and little or no accumulation of lipid and calcium. The type VI lesion contains fissure, hematoma and thrombus in the vascular wall. It is conceivable that decreasing the plasma cholesterol and lipid level would decrease the chance of atherosclerosis and arteriosclerosis. The prevention of hyperlipedmia and/or hypercholesterolemia can be resulted from either reducing the amount of the alimentary ingestion of cholesterol and lipids. Or inhibiting the absorption of cholesterol by inhibiting the activities of the convertal and/or acyl CoA-transferase enzymes (ACAT), thirdly, facilitating the rate of the degradation and clearance of cholesterol and lipids in the blood stream.

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- **Medical uses of a selective estrogen receptor modulator in combination with sex steroid precursors**

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  Patent Application Number: 20040157812

  Date filed: December 30, 2003

  Abstract: Novel methods for the medical treatment and/or inhibition of the development of osteoporosis, breast cancer, hypercholesterolemia, **hyperlipidemia** or atherosclerosis in susceptible warm-blooded animals including humans involving administration of selective estrogen receptor modulator particularly compounds having the general structure: 1and an amount of a sex steroid precursor selected from the group consisting of dehydroepiandrosterone, dehydroepiandrosterone sulfate, androst-5-ene-3.beta., 17.beta.-diol and compounds converted in vivo to one of the foregoing presursor. Further administration of bisphosphonates in combination with selective estrogen receptor modulators and/or sex steroid precursor is disclosed for the medical treatment and/or inhibition of the development of osteoporosis. Pharmaceutical

compositions for delivery of active ingredient(s) and kit(s) useful to the invention are also disclosed.

Excerpt(s): The present invention relates to a method for treating or reducing the likelihood of acquiring osteoporosis, hypercholesterolemia, **hyperlipidemia** or atherosclerosis using a novel combination therapy on susceptible warm-blooded animals, including humans. In particular, the combination includes administering a selective estrogen receptor modulator (SERM) and raising the patient's level of precursor to sex steroids, said precursor being selected from the group consisting of dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA-S), and androst-5-ene-3.beta.,17.beta.-diol (5-diol). The invention also relates to kits and pharmaceutical composition for practicing the foregoing combination. Man is thus unique, with some other primates, in having adrenals that secrete large amounts of the precursor steroids dehydroepiandrosterone sulfate (DHEA-S) and dehydroepiandrosterone (DHEA) which are converted into androstenedione (4-dione) and then into active androgens and/or estrogens in peripheral tissues (Labrie et al., In: Important Advances in Oncology. Edited by V. T. de Vita, S. Hellman, S. A. Rosenberg. J. B. Lippincott, Philadelphia, 193-217, 1985; Labrie, Mol. Cell.

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- **Method of reducing cholesterol**

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Patent Application Number: 20040097432

Date filed: November 3, 2003

Abstract: A method of treating elevated cholesterol levels, **hyperlipidemia** and/or hypercholesterolemia in a mammal includes administering an effective amount of theaflavins, thearubigins, and their mixture. The theaflavins include theaflavin and gallate esters of theaflavin, particularly those obtained from tea. The gallate esters include theaflavin-3-gallate, theaflavin-3'-gallate, and theaflavin-3,3'-digallate.

Excerpt(s): The present invention claims priority to U.S. Ser. No. 60/423,612 filed Nov. 4, 2002, the entire contents of which are incorporated herein by reference. The present invention relates to compositions containing theaflavins, thearubigins, or their combination for reducing cholesterol and for the treatment of **hyperlipidemia** and/or hypercholesterolemia. In particular, the present invention is directed to the method of reducing cholesterol or treating **hyperlipidemia** and/or hypercholesterolemia in a mammal by administering an anti-hyperlipidemia and/or anti-hypercholesterolemia effective amount of theaflavins, thearubigin, or their mixture. A desired composition includes a neutriceutically acceptable diluent or carrier and an active ingredient that is selected from the group consisting of theaflavin, a gallate ester of theaflavin, or their mixture, wherein the theaflavin and gallate ester of theaflavin are derived from tea. There is ongoing interest in reducing, treating or regulating cholesterol levels in the body because of the known link between **hyperlipidemia** and hypercholesterolamia and cardiovascular disease. A popular drug, Lipitor.RTM., is prescribed to lower the lipid content in hyperlipidemic people. Despite the success of Lipitor.RTM., many people desire a natural alternative to the widely available prescription drugs.

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- **Novel bicyclic compounds**

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  Patent Application Number: 20040127546

  Date filed: January 22, 2004

  Abstract: Compounds of the general formula (I): 1or a salt thereof, wherein R.sup.1 is hydrogen, hydroxyl or halogen; R.sup.2 is NHSO.sub.2CH.sub.3, SO.sub.2NHCH.sub.3 or the like; R.sup.5 and R.sup.6 each independently is hydrogen, C.sub.1-6 alkyl, optionally substituted phenyl or optionally substituted benzyl; X is NH, sulfur, oxygen or methylene; Y is oxygen, NR.sup.7, sulfur, methylene or a bond; and * represents an asymmetric carbon atom. The compounds are useful as a medicine for treating or preventing diabetes, obesity, **hyperlipidemia,** digestive diseases, depression or urinary disturbances.

  Excerpt(s): This invention relates to novel compounds which are useful as a medicine for treating and preventing diabetes, obesity, **hyperlipidemia,** digestive diseases, depression and urinary disturbances. Beta-adrenoreceptors are classified into three classes,.beta.1-adrenoreceptor,.beta.2-adrenoreceptor and.beta.3-adrenoreceptor, and it is recognized that stimulation of.beta.1 induces an increase in the heart rate and stimulation of.beta.2 induces a relaxation of the smooth muscle tissue, thereby resulting in lowering the blood pressure. It is also recognized that stimulation of.beta.3 facilitates the lipolysis in adipocytes, thereby resulting in increasing the thermogenesis. Therefore, compounds having.beta.3-agonist activity were shown to be useful as a medicine for treating and preventing diabetes, obesity and **hyperlipidemia** (Nature, vol. 309, pp. 163-165 (1984); Int. J. Obes. Relat. Metab. Disord., vol. 20, pp. 191-199 (1996); Drug Development Research, vol. 32, pp. 69-76 (1994); J. Clin. Invest., vol. 101, pp. 2387-2393 (1998)). Recently, it was shown that.beta.3-adrenoreceptor is expressed in the detrusor and a.beta.3-agonist induces a relaxation of the detrusor (J. Urinol., vol. 161, pp. 680-685 (1999); J. Pharmacol. Exp. Ther., vol. 288, pp. 1367-1373 (1999)). Some compounds showing a.beta.3-agonist activity have been known. Compounds having high selectivity or having low.beta.1- and.beta.2-stimulating activities are particularly required when their usefulness as a medicine is taken into consideration. This is because compounds having both.beta.1- and.beta.2-stimulating activities induce side effects such as increase in the heart rate and lowering of the blood pressure, as set forth above.

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- **Novel propionic acid derivatives**

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  Patent Application Number: 20040072690

  Date filed: October 10, 2003

  Abstract: A compound represented by the following formula (1) or a salt thereof: 1wherein R.sup.1 represents a C.sub.1-12 alkyl group, phenyl group, 1-naphthyl group

and the like, R.sup.2 represents a C.sub.2-12 alkyl group, (R.sup.3).sub.b represents 0 to 4 substituents such as a halogen atom, R.sup.4 represents a lower alkyl group, R.sup.5 represents hydrogen atom or a lower alkyl group, n represents an integer from 2 to 4, and X represents --NH-- or --O--, which has superior hypoglycemic action, hypolipidemic action and total cholesterol reducing action, and is useful as an active ingredient of a medicament for prophylactic and/or therapeutic treatment of diseases including diabetes mellitus, **hyperlipidemia** and the like.

Excerpt(s): The present invention relates to novel propionic acid derivatives which improve diabetes mellitus and/or **hyperlipidemia** and the like and also to pharmaceutical compositions comprising the same. For therapeutic treatment of diabetes mellitus, insulin preparations as injections or preparations of biguanide such as metformin hydrochloride or sulfonylurea such as tolbutamide as oral preparations have been conventionally used. However, the insulin preparations are inconvenient upon use as injections, whilst the biguanide preparations as oral preparations cause lactic acidosis and the sulfonylurea preparations have an adverse effect of severe hypoglycemia. Recently, thiazolidine-2,4-dione derivatives such as troglitazone (European Patent No. 139421), pioglitazone (European Patent No. 193256) and rosiglitazone (U.S. Pat. No. 5,002,953) have been focused, which are based on a novel mode of action of improvement of incompetence of insulin (insulin resistance) and free from the aforementioned adverse effects. However, troglitazone, pioglitazone and rosiglitazone have been reported to have side effects such as weight gain and edema, and troglitazone also has considerable problems, such as commercial distribution thereof has been discontinued due to high liver toxicity (J. Med. Chem., 35, 2617-2626, 1992). For these reasons, several thiazolidine-2,4-dione derivatives have been reported as described in Japanese Patent Unexamined Publication (Kokai) Nos. 10-139768 and 9-100280. However, no satisfactory therapeutic agent for insulin resistant diabetes mellitus is available at present. Hyperlipidemia is a state of higher blood levels of triglyceride, cholesterol and the like than normal levels, and considered as an object of therapeutic treatment because the disease is a major risk factor of ischemic diseases. As **hyperlipidemia** is known to cause atherosclerosis, reduction of blood cholesterol level and/or blood triglyceride level is particularly effective for prophylaxis and treatment of atherosclerosis. Atherosclerosis is also known as a cause of myocardial infarction, cerebral thrombosis, peripheral artery obstruction, and atherosclerosis obliterans (Nippon Rinsho, **Hyperlipidemia** (First volume), 529-629, 2001).

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- **Oestrogen fatty acid monoester as a hypolipidaemic and antidiabetic agent**

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Patent Application Number: 20040138193

Date filed: February 24, 2004

Abstract: Oleoyl estrone or estrone monooleate is a fatty-acid monoester of an estrogen which appear to be useful for the preparation of a medicament for the treatment and/or profilaxis of a human suffering from a metabolic disease selected from the group consisting of diabetes mellitus type 2, **hyperlipidemia** (hypertriacylglyceridemia, hyperlipoproteinemia, hypercholesterolemia) and the Metabolic Syndrome X associated

with glucose intolerance, hyperinsulinemia, or insulin resistance. Compared with insulin, oleoyl-estrone has the advantage of being aministered orally. The effectiveness of oleoyl-estrone as oral antidiabetic is conspicuous since it does not act as a simple hypoglycemic agent, but goes to the root of the problem lowering insulin resistance. The additional hypolipemic effect allows to extend its use for the treatment of dislipemias.

Excerpt(s): The present invention relates to new uses of known chemical compounds for fighting against metabolic diseases in humans. Diabetes mellitus is a widely extended pathology; it is found in two main forms: diabetes type 1 and diabetes type 2. In diabetes type 1, or juvenil diabetes, or insulin-dependent diabetes mellitus (IDDM), there is a severe lack of insulin production and release into the bloodstream. The lack of insulin is treated by periodical injections of the hormone; a failure to do so elicits a dramatic rise in blood glucose that leads to the presence of glucose in the urine and the massive passing of this urine. Diabetes type 2, or maturity-onset diabetes, or non-insulin-dependent diabetes mellitus (NIDDM) is more a consequence of the inability of the insulin present in the blood to effectively modulate the circulating glucose levels than to lack of the hormone. In NIDDM there is an "insulin resistance", the effects are not as dramatic as in IDDM and the diabetes is often combined with other physiological alterations, constituting the so-called "Metabolic Syndrome X" (sometimes referred as simply "X Syndrome" or "Metabolic Syndrome"), in which in addition to diabetes (hyperglycemia and hyperinsulinemia) the patients show other conditions, such as arterial hypertension and marked increases in blood lipids. Diabetes type 2 is more common than type 1 and is more susceptible to alternative treatment with diet and/or oral hypoglycemic drugs. There are several antidiabetic and/or hypoglycemic agents in the market such as insulin, biguanides, sulfonylurea derivatives, thiazolidinediones, and there are others (e.g. vanadium and tungsten compounds) proposed but not marketed yet. Nevertheless diabetes mellitus is still a major global health problem which is recognized by the World Health Organization to be reaching epidemic proportions. It is now the fourth leading cause of death in most developed countries and a disease that is increasing rapidly in countries undergoing industrialization. Diabetes mellitus is a disease in which there is a defective carbohydrate metabolism and is characterized by abnormally large amounts of sugar glucose in the blood and urine. Diabetes mellitus can eventually damage the eyes, kidneys, heart, and limbs, and can endanger pregnancy. Diabetes type 2 is usually associated with other metabolic diseases such as **hyperlipidemia,** hypertension and the so-called Metabolic Syndrome X. Therefore, the search for new therapeutical agents to fight these conditions is an active field of research.

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- **Stable pharmaceutical formulation comprising a HMG-CoA reductase inhibitor**

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  Patent Application Number: 20040072894

  Date filed: September 4, 2003

  Abstract: Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and derivatives and analogs thereof are known as HMG-CoA reductase inhibitors and are used as antihypercholesterolemic agents. The majority of them are produced by fermentation using microorganisms of different species identified as species belonging to Aspergillus,

Monascus, Nocardia, Amycolatopsis, Mucor or Penicillium genus, and some are obtained by treating the fermentation products using the methods of chemical synthesis or they are the products of total chemical synthesis.The aforementioned active substances may be destabilised by the environmental factors, their degradation may also be accelerated by interactions with other pharmaceutical ingredients, such as fillers, binders, lubricants, glidants and disintegrating agents, therefore the pharmaceutical ingredients and the process for preparation of the pharmaceutical formulation should be meticulously chosen to avoid the aforementioned undesired interactions and reactions.The present invention relates to a stable solid pharmaceutical formulation for the treatment of hypercholesterolemia and **hyperlipidemia.** More precisely, the present invention relates to the new stable solid pharmaceutical formulation containing as an active ingredient a HMG-CoA reductase inhibitor, such as atorvastatin, pravastatin, fluvastatin and cerivastatin or pharmaceutically acceptable salts thereof.

Excerpt(s): The present invention relates to a new stable solid pharmaceutical formulation which is particularly suitable for the treatment of hypercholesterolemia and **hyperlipidemia.** More precisely, the present invention relates to the new stable solid pharmaceutical formulation containing as an active substance a HMG-CoA reductase inhibitor, such as atorvastatin, pravastatin, fluvastatin and cerivastatin, or pharmaceutically active salts thereof. Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, fluvastatin and cerivastatin, derivatives and analogs thereof are known as HMG-CoA reductase inhibitors and are used as antihypercholesterolemic agents. The majority of them are produced by fermentation using microorganisms of different species identified as species belonging to Aspergillus, Monascus, Nocardia, Amycolatopsis, Mucor or Penicillium genus. Some are obtained by treating the fermentation products using the methods of chemical synthesis like simvastatin or they are the products of total chemical synthesis like fluvastatin, atorvastatin and cerivastatin. The purity of the active substance is an important factor for manufacturing a safe and effective pharmaceutical formulation. Maximum possible purity of the product is of particular importance if the pharmaceutical product must be taken on a longer term basis in the treatment or prevention of **high cholesterol** levels in blood. Accumulation of impurities from drugs of a lower level of purity may cause a variety of side effects during treatment. Besides impurities, that cannot be completely eliminated in the process of preparation of the active substance, degradation products occurring by subjecting the final pharmaceutical formulation to various environmental factors such as temperature, moisture, low pH and light, may also impose a problem. HMG-CoA reductase inhibitors occurring in the form of salts in the final pharmaceutical formulation, such as atorvastatin, pravastatin, fluvastatin and cerivastatin, are particularly sensitive to an acidic environment in which hydroxy acids are degraded into a lactone.

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- **Therapeuctic combination**

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  Patent Application Number: 20040048906

  Date filed: August 8, 2003

Abstract: This invention relates to pharmaceutical combinations of amlodipine or a pharmaceutically acceptable acid addition salt thereof and atorvastatin or a pharmaceutically acceptable salt thereof, kits containing such combinations and methods of using such combinations to treat subjects suffering from angina pectoris, atherosclerosis, combined hypertension and **hyperlipidemia** and to treat subjects presenting with symptoms of cardiac risk, including humans. This invention also relates to additive and synergistic combinations of amlodipine and atorvastatin whereby those synergistic combinations are useful in treating subjects suffering from angina pectoris, atherosclerosis, combined hypertension and **hyperlipidemia** and those subjects presenting with symptoms of cardiac risk, inducing humans.

Excerpt(s): This invention relates to pharmaceutical combinations of amlodipine and pharmaceutically acceptable acid addition salts thereof and atorvastatin and pharmaceutically acceptable salts thereof, kits containing such combinations and methods of using such combinations to treat subjects suffering from angina pectoris, atherosclerosis, combined hypertension and **hyperlipidemia** and to treat subjects presenting with symptoms of cardiac risk including humans. This invention also relates to additive and synergistic combinations of amlodipine and atorvastatin whereby those additive and synergistic combinations are useful in treating subjects suffering from angina pectoris, atherosclerosis, combined hypertension and **hyperlipidemia** and those subjects presenting with symptoms or signs of cardiac risk, including humans. The conversion of 3hydroxy-3methylglutaryl-coenzyme A (HMG-CoA) to mevalonate is an early and rate-limiting step In the cholesterol biosynthetic pathway. This step is catalyzed by the enzyme HMG-CA reductase. Statins inhibit HMG-CA reductase from catalyzing this conversion. As such, statins are collectively potent lipid lowering agents. and is disclosed in U.S. Pat. No. 4,681,893, which is incorporated herein by reference.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Therapeutic applications of estrogenic carboxylic acids**

  Inventor(s): Adler, Stuart R.; (Creve Coeur, MO), Banz, William J.; (Carterville, IL), Dandliker, Walter B.; (La Jolla, CA), Hou, Yuqing; (Carbondale, IL), Meyers, Cal Y.; (Carbondale, IL), Winters, Todd A.; (Murphysboro, IL)

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  Patent Application Number: 20040116398

  Date filed: July 22, 2003

  Abstract: Provided are methods employing estrogenic compounds for: repressing weight gain or reducing weight in male patients; treating or preventing prostate cancer and peri- or post-menopausal symptoms; treating estrogen-responsive conditions that no longer respond to treatment with conventional steroidal estrogens; treating or preventing estrogen-responsive uterine cancer, breast cancer, and ovarian follicle atresia; inducing ovulation to increase fertility; oral contraception; treating or preventing diseases or conditions caused or prolonged by free radicals; treating or preventing cardiovascular disease, **hyperlipidemia** or hypercholesterolemia, and hyperglycemia; improving body fat distribution; and treating or preventing Alzheimer's disease, osteoporosis, and pattern baldness. Also provided are methods for treating or preventing prostatic diseases including benign prostate hyperplasia and other related conditions, androgen-responsive pathological conditions in males, and methods for male birth control and chemical castration, employing estrogenic carboxylic acids.

Excerpt(s): This application is a division of U.S. patent application Ser. No. 09/338,823, filed Jun. 23, 1999, which claims priority from U.S. Provisional Patent Application Serial No. 60/090,344, filed Jun. 23, 1998. The present invention relates to the field of pharmaceutical therapeutics. More specifically, the present invention relates to the use of estrogenic carboxylic acids in improved therapies for the treatment of a variety of symptoms and disease conditions in mammals. The present invention also relates to the field of chemical synthesis, more specifically, the synthesis of estrogenic carboxylic acids. Estrogens, such as (+)-17.beta.-estradiol (E2), have physiological effects on males as well as females. In addition to their activity in reproductive tissue, they promote rapid weight gain in specific species, and have been marketed to fatten livestock quickly. Trenkle, AH: "The Mechanisms of Action of Estrogens in Feeds on Mammalian and Avian Growth." Proceedings of a Symposium: The Use of Drugs in Animal Feed. National Academy of Science, Washington D.C. 150-164 (1968); Meyers, U.S. Pat. No. 5,420,161. Estrogens have long been prescribed for their beneficial effects by reducing susceptibility to osteoporosis and ameliorating menopausal and postmenopausal symptoms. Evans S F, Davie M W: "Low and Conventional Dose Transdermnal Oestradiol Are Equally Effective at Preventing Bone Loss In Spine and Femur at All Post-Menopausal Ages." Clin Endocrinol. 44:79-84 (1996); Agarwal S K, Judd H L: "Menopause." Curr Ther Endocrinol Metab. 6:624-631 (1997). Long-term clinical studies suggest that estrogens may be beneficial in promoting cardiovascular health. Wilson P W: "The Impact of Estrogen on Cardiovascular Disease." Perspective Studies: The Framingham Study. Postgrad Med 51-53:89-90 (1989). More recently, estrogens have shown promise as an adjunct in treatment of Alzheimer's disease. Filley C M: "AlZheimer's Disease in Women." Am J Obstet Gynecol 176:1-7 (1997). Unfortunately, some estrogenic compounds administered in therapeutic doses are suspected carcinogens in target tissues including breast and uterus. Persson I: "Cancer Risk in Women Receiving Estrogen-Progestin Replacement Therapy." Maturitas 23:S37-45 (1996).

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 hyperlipidemia, 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 “hyperlipidemia” (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 hyperlipidemia.

You can also use this procedure to view pending patent applications concerning hyperlipidemia. 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 5. BOOKS ON HYPERLIPIDEMIA

Overview

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

- **Pediatric Nutrition Handbook, Fourth Edition**

  Source: Elk Grove Village, IL: American Academy of Pediatrics. 1998. 833 p.

  Contact: Available from American Academy of Pediatrics. P.O. Box 927, 141 Northwest Point Boulevard, Elk Grove Village, IL 60009-0927. (800) 433-9016. PRICE: $47.95 (members) plus $6.25 shipping and handling; $52.95 for nonmembers; plus $8.95 shipping and handling. ISBN: 1581100051.

  Summary: Assessment of nutritional status and providing dietary advice and nutritional support are important and increasingly prominent components of the practice of those who provide health care for infants, children, and adolescents. This handbook serves as a ready desk reference on the nutritional requirements and impact of nutritional status on the health of infants, children, and adolescents. Forty-three chapters cover breastfeeding; formula feeding of term infants; supplemental foods for infants; vitamin

and mineral supplement needs of healthy children in the United States; feeding from age 1 year to adolescence; adolescent nutrition; the nutritional needs of preterm infants; the recognition and management of pediatric swallowing disorders; energy; proteins; carbohydrate and dietary fiber; fats and fatty acids; calcium, phosphorus, and magnesium; trace elements; vitamins; infant nutrition and the development of gastrointestinal function; parenteral nutrition; enteral nutrition; nutrition and oral health; sports nutrition; community nutrition services for children; current legislation and regulations regarding infant formulas; assessment of nutritional status; failure to thrive; gastrointestinal disease, persistent diarrheal disease, and malabsorption; oral rehydration therapy and posttreatment feeding after enteritis; iron deficiency; inborn errors of metabolism; dietary management of diabetes mellitus; hypoglycemia; **hyperlipidemia;** obesity in children; food hypersensitivity; nutrition and immunity; nutritional management of children with a chronic illness; nutrition in children with HIV infection; diet in the prevention of cancer or hypertension; food labeling; nutritional aspects of vegetarian diets; fast foods, organic foods and megavitamins; food safety; and new food ingredients. Extensive appendices and a subject index conclude the volume.

- **Moving Away from Diets: New Ways to Heal Eating Problems and Exercise Resistance**

  Source: Lake Dallas, TX: Helm Seminars, Publishing. 1996. 174 p.

  Contact: Available from Helm Seminars, Publishing. P.O. Box 1295, Lake Dallas, TX 75065. (940) 497-3558. PRICE: $34.95 plus $4.00 shipping and handling. ISBN: 0963103350.

  Summary: Because no one program is the solution to every person's food and weight concerns, this book provides a general framework of nondiet weight, hunger, and fitness management. The foreword notes that clinical studies and observations support the association of weight loss with improvement of hypertension, diabetes, and **hyperlipidemia.** According to the authors, dieting is an ineffective means of weight loss. They point out that in 95 percent of cases, lost weight is regained within 5 years. The book challenges the belief that it is impossible to be fit and fat at the same time; that all large people must lose weight and are in poor health; that everyone can lose weight if they simply adhere to the proper diet and to a regular exercise program; and that the main reason people regain lost weight is because they fail to comply with prescribed diets or make long-term commitments to weight loss. Ten chapters, divided into three parts, discuss the importance of size acceptance by both providers and consumers of health care; how the dieting cycle contributes to a person's eating problems; the origins and treatment strategies for exercise resistance; counseling and implementation strategies; and marketing the nondiet approach. Chapters 4 through 6 provide information on HungerWork, a treatment approach which helps clients appreciate natural signs of hunger, appetite, fullness, and satiety. Chapters 8 and 9 provide case studies. A list of resources concludes most chapters. An index and sample promotional items designed to illustrate successful programming concepts and ideas conclude the book. 31 figures. 1 table. 169 references. (AA-M).

- **Cardiac Dysfunction in Chronic Uremia**

  Source: Norwell, MA: Kluwer Academic Publishers. 1992. 231 p.

  Contact: Available from Kluwer Academic Publishers. P.O. Box 358, Accord Station, Hingham, MA 02018-0358. (617) 871-6600. PRICE: $145 plus shipping and handling.

Summary: Cardiac disease is the major cause of death in dialysis patients, accounting for over one-third of deaths. This book focuses on myocardial function and dysfunction in chronic uremia. It is written for practicing and training nephrologists, cardiologists, and internists, and for research workers in the field. The first section comprises five chapters that provide an overview of the burden of illness associated with cardiac disease in end-stage renal disease and a review of clinical epidemiological aspects of various cardiac diseases that occur in renal patients. The second section discusses abnormalities of left ventricular contractility and mass, and the factors that predispose to both systolic and diastolic disorders. The importance of hypertension, anemia, hyperparathyroidism, **hyperlipidemia,** and diabetes mellitus is reviewed. The final section concentrates on therapeutics. Data and opinion on management of congestive heart failure, cardiomyopathy, coronary artery disease, hypertension, and arrhythmias are provided. Each chapter includes numerous references and a subject index is appended to the volume. (AA-M).

- **Pathogenetic and Therapeutic Aspects of Chronic Renal Failure**

  Source: New York, NY: Marcel Dekker, Inc. 1997. 242 p.

  Contact: Available from Marcel Dekker, Inc. 270 Madison Avenue, New York, NY 10016. (212) 696-9000. Fax (212) 685-4540. PRICE: $115.00. ISBN: 0824798945.

  Summary: This book is based on an international workshop, Chronic Renal Failure: Pathogenetic and Therapeutic Aspects, held in Berlin in May 1996. The first part of the book deals with arterial hypertension, **hyperlipidemia,** and metabolic acidosis as factors that accelerate the progression of chronic renal failure (CRF) and with the effect of dietary protein restriction as a measure to slow the advance of renal insufficiency. The second part addresses the etiology and pathophysiology of myocardial hypertrophy in general, and especially in uremia, and the influence of the dialysis regimen on the development of myocardial hypertrophy. The final section discusses the correction of renal anemia via treatment with recombinant human erythropoietin (rhEPO), with special emphasis on its effects on cardiac function and hypertrophy and on the function of parts of the endocrine system. Also included are an analysis of the use of rhEPO in renal transplant patients and an overview of the problems of iron supplementation in rhEPO treatment. The 17 chapters, each written by experts in the field, include reference lists; a subject index concludes the book.

- **Medications for the Treatment of Diabetes**

  Source: Alexandria, VA: American Diabetes Association. 2000. 190 p.

  Contact: Available from American Diabetes Association (ADA). Order Fulfillment Department, P.O. Box 930850, Atlanta, GA 31193-0850. (800) 232-6733. Fax (770) 442-9742. Website: www.diabetes.org. PRICE: $14.95 plus shipping and handling. ISBN: 1580400612.

  Summary: This book presents an overview of the medications used to treat patients who have type 1 or type 2 diabetes and provides an individual summary of each class of drug and its role in the treatment of diabetes. Chapter one discusses the use of insulin for type 1 diabetes. Topics include insulin sources; insulin pharmacology; insulin storage, mixing, and administration; insulin dosing regimens; insulin use in diabetic ketoacidosis, parenteral nutrition, and pump therapy and among pregnant women, infants, and children; and the role of glucagon in type 1 diabetes. Chapter two reviews the use of insulins, sulfonylureas, thiazolidinediones, meglitinides, biguanides, and alpha glucosidase inhibitors in the treatment of type 2 diabetes. These classes of

medications are discussed in terms of mechanisms of action, efficacy of monotherapy and combination therapy, effects on lipid profiles, common side effects, contraindications for use, and patient adherence to the regimens. Chapters three through seven discuss sulfonylureas, alpha glucosidase inhibitors, glitazones, meglitinide products, and biguanides in terms of pharmacology, indications for use, dosing considerations, special populations, contraindications, warnings, precautions, adverse effects, drug interactions, and clinical effects. Chapter eight focuses on insulin use in type 2 diabetes and gestational diabetes. Topics include indications for use, rationale and strategies for oral agent insulin therapy, insulin monotherapy in type 2 diabetes, and intensive insulin therapy. Chapters nine and 10 examine the treatment of hypertension and **hyperlipidemia** in patients who have diabetes, focusing on the goals of treatment, nonpharmacological interventions, and pharmacological treatments. The final chapter describes some medications currently being studied that will possibly be approved to treat diabetes or its complications. 6 figures. 31 tables. Numerous references.

- **Origins and Consequences of Obesity**

  Source: Somerset, NJ: John Wiley and Sons, Inc. 1996. 278 p.

  Contact: Available from John Wiley and Sons, Inc. One Wiley Drive, Somerset, NJ 08875. (800) 225-5945 or (732) 469-4400. Fax (732) 302-2300. Website: www.wiley.com. PRICE: $90.00 plus shipping and handling. ISBN: 0471965065.

  Summary: This book presents the papers given at a symposium that brought together an international and interdisciplinary group of experts on all aspects of the origins, consequences, and treatment of obesity. The health consequences of being obese or overweight, which include diabetes, hypertension, and **hyperlipidemia,** are among the most common health problems in industrialized nations. Speakers discussed the epidemiology of obesity, obesity among people living in Caribbean nations, and obesity in peoples of the African diaspora. Other presenters focused on the metabolic consequences of obesity and body fat pattern, diabetes, obesity and cardiovascular disease, the genetics of obesity in humans, and early-life nutritional influences upon obesity and body proportions. The presentation on diabetes examined the relationship between obesity and type 2 diabetes. It also reviewed clinical and epidemiological studies on insulin resistance in central obesity, addressed pathogenetic considerations, and discussed endocrine regulation of body fat distribution and endocrine regulation of insulin sensitivity. The presentation also examined evidence for the view that endocrine abnormalities may be diabetogenic via the induction of insulin resistance. Remaining speakers provided information on behavioral physiological interactions in the control of food intake, obesity and metabolic efficiency, socioeconomic status and obesity, the economic and psychosocial consequences of obesity, obesity and physical activity, and preventive and management strategies for obesity. A discussion followed each presentation, and two general discussion sessions were conducted. The book concludes with an index of contributors and a subject index. 1 appendix. 38 figures. 26 tables. Numerous references.

- **Obesity**

  Source: Hagerstown, MD: J.B. Lippincott Company. 1992. 805 p.

  Contact: Available from J.B. Lippincott Company. P.O. Box 1580, Hagerstown, MD 21741. (800) 777-2295. PRICE: $79.50; plus shipping and handling. ISBN: 0397509995.

Summary: This book provides an overview of fundamental research and clinical aspects of obesity. The 66 chapters of the book, each written by preeminent scientists and clinicians, are presented in 11 sections: fat metabolism; assessment of body composition; energy metabolism; animal models of obesity; general aspects of human obesity; hunger satiety and mood; associated health impairments; health impairments associated with abdominal distribution of adipose tissue; special forms of obesity; nonpharmacologic treatment of obesity; and the pharmacologic treatment of obesity. Chapters related to diabetes include a chapter on glucose metabolism in obesity and Type II diabetes and chapters discussing **hyperlipidemia,** cardiovascular disease, and hypertension. Each chapter includes numerous references to primary sources, and a subject index concludes the volume.

- **Advances of Diabetes Mellitus in East Asia**

  Source: Amsterdam, Netherlands: Elsevier Science. 1997. 288 p.

  Contact: Available from Elsevier Science. P.O. Box 945, New York, NY 10159-0945. (888) 437-4636 or (212) 633-3730. Fax (212) 633-3680. E-mail: usinfo-f@elsevier.com. PRICE: $184.50. ISBN: 0444826645.

  Summary: This book summarizes recent experimental and clinical developments and results which were reported during the proceedings of the 5th China-Japan Symposium on Diabetes Mellitus. The papers are presented in nine categories: plenary lectures; invited lecture; epidemiology; etiology and metabolism; insulin secretion; glycation; obesity and **hyperlipidemia;** complications; and treatment and education. Specific topics addressed include the prevalence of diabetes and its risk factors in China; incidence of IDDM in Beijing; treatment trends in Japan; malnutrition-related diabetes; current clinical research; intensive insulin therapy; Metformin; Chinese herbal drugs; patient education; and quality of life. An index of authors concludes the book. (AA-M).

- **Handbook of Diabetes, Second Edition**

  Source: Malden, MA: Blackwell Science, Inc. 1999. 220 p.

  Contact: Available from Blackwell Science, Inc. 350 Main Street, Commerce Place, Malden, MA 02148. (800) 215-1000 or (617) 388-8250. Fax (617) 388-8270. E-mail: books@blacksci.com. Website: www.blackwell-science.com. PRICE: $60.95. ISBN: 0632055049.

  Summary: This handbook covers a wide spectrum of information on diabetes mellitus. The handbook includes an introduction and 31 topical chapters: the history of diabetes, diagnosis of diabetes, classification, public health aspects, normal physiology of insulin secretion and action, the epidemiology and etiology of type 1 diabetes, the epidemiology and etiology of type 2 diabetes, other types of diabetes, assessing control in diabetes, the management of type 1 diabetes, the management of type 2 diabetes, diabetic ketoacidosis and hyperosmolar non-ketotic coma, hypoglycemia (low blood glucose levels), control and complications, diabetic eye disease (retinopathy), diabetic nephropathy (kidney disease), diabetic neuropathy (nerve disease), **hyperlipidemia** (high levels of blood fats) in diabetes, hypertension (high blood pressure) in diabetes, macrovascular disease in diabetes, the diabetic foot, sexual problems in diabetes, gastrointestinal problems in diabetes, the skin in diabetes, psychological and psychiatric problems in diabetes, some intercurrent problems (exercise, drugs, infection, surgery), pregnancy and diabetes, diabetes in children, diabetes in the elderly, lifestyle considerations (driving, employment, smoking, travel), and the organization of diabetes care. The handbook design includes information presented in small chunks, with

numerous color illustrations, charts, and photographs to make the information more accessible. A detailed subject index concludes the book.

- **Guidelines for the Nutritional Intervention of the Adult Dialysis Patient**

  Source: Marina del Rey, CA: R and D Laboratories, Inc. 1990. 88 p.

  Contact: Available from R and D Laboratories, Inc. 4640 Admiralty Way, Suite 710, Marina del Rey, CA 90292. (800) 338-9066. PRICE: Contact directly for current price.

  Summary: This handbook is designed to assist the renal dietitian through the complex steps of evaluating the nutrition status of a dialysis patient. The guidelines are arranged by individual diagnoses or problems, and are based primarily on laboratory chemistries, presented as a quick reference. Expected patient outcome criteria are listed for each problem, along with a list of appropriate dietary interventions. A patient education documentation sheet suitable for use in the medical record is provided for each of the problems. Topics include **hyperlipidemia,** body weight changes, hyper-and hypocalcemia, hyperphosphatemia, elevated BUN, depressed serum albumin, hyperkalemia, fluid overload, and low hematocrit. 18 references.

- **Pediatric Nutrition Handbook. 3rd ed**

  Source: Elk Grove Village, IL: American Academy of Pediatrics. 1993. 472 p.

  Contact: Available from American Academy of Pediatrics. P.O. Box 927, 141 Northwest Point Boulevard, Elk Grove Village, IL 60009-0927. (800) 433-9016. PRICE: $47.95 (members) plus $6.25 shipping and handling; $52.95 for nonmembers; plus $8.95 shipping and handling. ISBN: 0910761388.

  Summary: This handbook serves as a ready desk reference on the nutritional requirements and impact of nutritional status on the health of infants, children, and adolescents. Thirty-five chapters cover breastfeeding; formula feeding of term infants; supplemental foods for infants; vitamin and mineral supplement needs of healthy children in the United States; feeding from age 1 year to adolescence; adolescent nutrition; the nutritional needs of preterm infants; energy; proteins; carbohydrate and dietary fiber; fats and fatty acids; calcium, phosphorus, and magnesium; trace elements; vitamins; infant nutrition and the development of gastrointestinal function; parenteral nutrition; nutrition and oral health; community nutrition services for children; current legislation and regulations regarding infant formulas; assessment of nutritional status; failure to thrive; gastrointestinal disease, chronic diarrhea, and malabsorption; oral fluid therapy and posttreatment feeding after enteritis; iron deficiency; inborn errors of metabolism; diabetes mellitus; hypoglycemia; **hyperlipidemia;** obesity; food hypersensitivity; nutrition and infection; diet in the prevention of cancer or hypertension; nutritional aspects of vegetarian diets; fast foods, organic foods, and megavitamins; and food additives. Extensive appendices and a subject index conclude the volume.

- **Getting to the Heart of It**

  Source: Boston, MA: Joslin Diabetes Center. 1999. 29 p.

  Contact: Available from Joslin Diabetes Center. One Joslin Place, Boston, MA 02215. (800) 344-4501 or (508) 583-3240. Fax (617) 732-2562. Website: www.joslin.harvard.edu. PRICE: $9.95 each; plus shipping and handling. Order number JDC430.

Summary: This self-learning interactive workbook presents steps people who have diabetes can take to keep their heart and blood vessels healthy. The workbook identifies major risk factors for heart disease, suggests how people can set goals to minimize these risks, and provides people with strategies for changing behavior by developing and following an individualized action plan. Chapters use a question and answer format to provide information about diabetes, high blood fats, high blood pressure, protein in the urine, inactivity, obesity, and smoking. Chapter one presents an overview of diabetes. The chapter explains what diabetes is, how to determine high blood sugar levels, how to check blood sugar levels, what complications are caused by high blood sugar, and what steps people can take to control blood sugar levels. Chapter two focuses on high blood fats. Questions deal with what **hyperlipidemia** is and how it is diagnosed, the foods that contain fat and cholesterol, how **hyperlipidemia** relates to diabetes and to cardiovascular disease, the complications caused by **hyperlipidemia,** and how **hyperlipidemia** can be prevented and treated. The focus of chapter three is on high blood pressure. Topics include the diagnosis of hypertension, the relationship between hypertension and diabetes and hypertension and cardiovascular disease, the complications caused by hypertension, and ways to lower blood pressure. Chapter four discusses protein in the urine, focusing on what proteinuria is, how it is diagnosed, how it relates to diabetes and cardiovascular disease, the complications caused by proteinuria, how people can reduce their risk for proteinuria, and the steps people can take to slow down or prevent kidney problems. Remaining chapters address the issues of inactivity, obesity, and smoking. Topics include how these factors relate to diabetes and cardiovascular disease and how people can become more active, lose weight, and stop smoking. The book also includes a body mass index chart and charts for personal recordkeeping.

- **Medical Care of the Liver Transplant Patient**

  Source: Oxford, England: Blackwell Science Ltd. 1997. 409 p.

  Contact: Available from Blackwell Science, Inc. 238 Main Street, Cambridge, MA 02142. (800) 215-1000 or (617) 876-7000. Fax (617) 492-5263. PRICE: $95.00. ISBN: 0865425248.

  Summary: Written for physicians, nurses, and other health professionals who care for liver transplant patients, this book answers practical questions about drugs and drug interactions, complications, and the special medical concerns and primary care needs of such patients. The book covers selection and referral of patients for transplantation and post-transplant management, as well as problems that occur frequently in the course of pre-and postoperative management. Special sections on psychiatric evaluation and social rehabilitation reinforce the theme of a comprehensive approach. The authors support the reintegration of the care of liver transplant patients into the community-based practice of medicine. Chapters also cover the timing of transplantation, fulminant hepatic failure, management of portal hypertension and biliary disease prior to transplantation, patients with alcoholic liver disease, financial considerations, procurement and allocation of donor livers, rejection or infection, vascular aspects of liver transplantation, biliary complication post-transplantation, histopathology and research. Renal function, obesity and **hyperlipidemia** after liver transplantation, social rehabilitation, pharmacology of immunosuppressive drugs and drug interactions, and liver transplantation in children are covered as well. Each chapter concludes with 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 "hyperlipidemia" at online booksellers' Web sites, you may discover non-medical books that use the generic term "hyperlipidemia" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "hyperlipidemia" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **Drug Treatment of Hyperlipidemia** by Basil M. Rifkind; ISBN: 0824785126; http://www.amazon.com/exec/obidos/ASIN/0824785126/icongroupinterna

Chapters on Hyperlipidemia

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

- **Causes, Consequences, and Treatment of Hyperlipidemia in Patients with Renal Disease**

  Source: in Andreucci, V.E.; Fine, L.G., eds. International Yearbook of Nephrology 1991. Hingham, MA: Kluwer Academic Publishers. 1990. p. 179-196.

  Contact: Available from Kluwer Academic Publishers. P.O. Box 358, Accord Station, Hingham, MA02018-0358. (617) 871-6600. PRICE: $135.00. ISBN: 0792310020.

  Summary: It is well-established that abnormalities in lipoprotein metabolism are associated with an increased risk for atherosclerotic cardiovascular disease. This chapter, from an international yearbook in nephrology, discusses the causes, consequences, and treatment of **hyperlipidemia** in patients with renal disease. Topics include: normal lipoprotein metabolism and primary hyperlipidemias; **hyperlipidemia** and the nephrotic syndrome; **hyperlipidemia** in chronic renal failure and hemodialysis; **hyperlipidemia** in continuous ambulatory peritoneal dialysis (CAPD); and **hyperlipidemia** in renal transplant recipients. 5 figures. 2 tables. 94 references.

- **Management of the Hyperlipidemia of the Nephrotic Syndrome**

  Source: in Andreucci, V.E. International Yearbook of Nephrology 1990. Hingham, MA: Kluwer Academic Publishers. 1990. p. 53-69.

  Contact: Available from Kluwer Academic Publishers. P.O. Box 358, Accord Station, Hingham, MA02018-0358. (617) 871-6600.

Summary: This chapter summarizes and discusses various aspects associated with the effective management of patients with **hyperlipidemia** of the nephrotic syndrome, a syndrome representing a renal disorder characterized by proteinuria, hypoalbuminemia, sometimes edema, and **hyperlipidemia.** Specific attention is given to mechanisms of nephrotic **hyperlipidemia** (NH) (hypercholesterolemia; hypertriglyceridemia) and to drug therapy of NH (bile acid resins; nicotinic acid; 3-hydroxy-3- methylglutaryl coenzyme A reductase inhibitors; fibric acids; probucol). The utility of combined drug therapy also is discussed. 56 references.

CHAPTER 6. PERIODICALS AND NEWS ON HYPERLIPIDEMIA

Overview

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

News Services and Press Releases

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

- **Fat intake not linked to hyperlipidemia in diabetic children**
  Source: Reuters Medical News
  Date: May 13, 2003
- **Olanzapine use linked to hyperlipidemia in schizophrenics**
  Source: Reuters Medical News
  Date: December 04, 2002

- **New diagnostic criteria for familial combined hyperlipidemia proposed**
  Source: Reuters Medical News
  Date: March 01, 2002
- **Dietary fat restriction in children with hyperlipidemia may be overzealous**
  Source: Reuters Medical News
  Date: November 14, 2001
- **Simvastatin recommended as first-line therapy for hyperlipidemia in UK**
  Source: Reuters Medical News
  Date: March 27, 2001

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

Newsletter Articles

Use the Combined Health Information Database, and limit your search criteria to "newsletter articles." Again, you will need to use the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter Article." Type "hyperlipidemia" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months. The following is a typical result when searching for newsletter articles on hyperlipidemia:

- **Preventing Childhood Obesity: a Multipronged Approach**

  Source: WIN Notes. pp. 4-5. Summer 2001.

  Contact: Weight-control Information Network. 1-877-WIN-4627.

  Summary: At the 2000 annual meeting of the American Obesity Association (AOA), many experts expressed concern about the rise in childhood obesity. The percentage of overweight and obese children aged 6 to 17 has doubled in the past 30 years, with a corresponding rise in the incidence of type 2 diabetes, hypertension, cardiovascular disease, **hyperlipidemia,** and psychosocial disorders among these children. Many of those who spoke at the AOA meeting stressed the need to develop effective strategies to reverse the rise in childhood obesity. William Dietz, M.D., Ph.D., at the Centers for Disease Control and Prevention (CDC), described how family, community, health care providers, and media influence could all help increase physical activity and support good nutrition among children. Howell Wechsler, Ed.D., M.P.H., a CDC scientist, outlined strategies for shaping the psychosocial environment of a school to support physical activity and healthy eating. Morgan Downey, J.D., AOA's executive director, suggested that health care professionals speak with local PTAs and school boards to 'connect the dots' between fast food lunches, fewer physical education classes, and high rates of childhood obesity with the accompanying chronic health problems. Marc Jacobson, M.D., Director of the Center for Atherosclerosis Prevention at Schneider Children's Hospital in New York, spoke about the pediatrician's role in obesity prevention. For children 2 to 7 years old, weight maintenance is the goal, unless other health complications exist. For those children age 8 and older, weight loss is targeted only for those children whose BMI is above the 95th percentile, unless complications are present in those above the 85th percentile.

- **Researchers Investigate New Obesity-related Disease**

  Source: WIN Notes. p. 4, 10. Summer 2002.

  Contact: Weight-control Information Network, 1 WIN Way, Bethesda, MD 20992-3665. (202) 828-1025.

Summary: Nonalcoholic steatohepatitis (NASH) is a liver disease that occurs most often in adults over the age of 40 who are overweight or have diabetes, insulin resistance, or **hyperlipidemia.** NASH resembles alcoholic liver disease, however, people with NASH drink little or no alcohol. Although most people with NASH are middle-aged, obese, and diabetic, the disease may also strike children and normal-weight adults without diabetes. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is funding a 5-year study of NASH in hopes of finding prevention and treatment approaches. Scientists are uncertain about what causes NASH, but believe it is a combination of insulin resistance and oxidative stress. NIDDK plans to establish a NASH Clinical Research Network to study this poorly understood disease. Researchers will investigate NASH's origin, contributing factors, natural history, and complications. They hope to identify safe and effective methods to prevent and treat this increasingly common disease.

- **An Alternative to Traditional Weight Management Programs: Health at Every Size (HAES)**

  Source: SCAN'S Pulse. 23(1):12-14. Winter 2004.

  Contact: Sports, Cardiovascular, and Wellness Nutritionists. American Dietetic Association. 120 South Riverside Plaza, Suite 2000. Chicago, IL 60606-6995. www.SCANDPG.org.

  Summary: The Health at Every Size (HAES) movement focuses on health enhancement, size- and self-acceptance, the pleasure of eating well, the joy of movement, and an end to weight stigmatization. Preliminary research suggests that HAES can help reduce anxiety, normalize eating behavior, and improve self-esteem in chronic dieters. When used with individuals with type 2 diabetes, **hyperlipidemia,** and hypertension, HAES works to improve self-esteem, decrease health risks, increase self-control, and reduce guilt. HAES focuses on health promotion at a client's current weight with minimal, if any, attention paid to weight. Removing the focus from weight does not mean ignoring health risks and medical problems. The article ends with a case study of working with an obese woman using the HAES approach.

Academic Periodicals covering Hyperlipidemia

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to hyperlipidemia. In addition to these sources, you can search for articles covering hyperlipidemia 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 7. 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 hyperlipidemia. 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 hyperlipidemia. 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 hyperlipidemia:

Cholestyramine

- **Oral - U.S. Brands:** Questran; Questran Light
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202137.html

Clofibrate

- **Systemic - U.S. Brands:** Abitrate; Atromid-S
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202150.html

Colesevelam

- **Oral-Local - U.S. Brands:** Welchol
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500157.html

Colestipol

- **Oral - U.S. Brands:** Colestid
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202161.html

Ezetimibe

- **Systemic - U.S. Brands:** Zetia
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500435.html

Fenofibrate

- **Systemic - U.S. Brands:** Lofibra; Tricor
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203516.html

HMG-CoA Reductase Inhibitors

- **Systemic - U.S. Brands:** Baycol; Lescol; Lipitor; Mevacor; Pravachol; Zocor
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202284.html

Laxatives

- **Oral - U.S. Brands:** Agoral; Alophen; Alphamul; Alramucil Orange; Alramucil Regular; Bisac-Evac; Black-Draught; Black-Draught Lax-Senna; Carter's Little Pills; Cholac; Citroma; Citrucel Orange Flavor; Citrucel Sugar-Free Orange Flavor; Colace; Constilac; Constulose; Correctol; Correctol Caplets; Correctol Herbal Tea; Correctol Stool Softener Soft Gels; D.O.S. Softgels; DC Softgels; Diocto; Diocto-C; Dioeze; Diosuccin; Docu-K Plus; DOK; DOK Softgels; Dr. Caldwell Senna Laxative; D-S-S; D-S-S plus; Dulcolax; Emulsoil; Enulose; Epsom salts; Equalactin; Evac-U-Gen; Ex-Lax; Ex-Lax Chocolate; FemiLax; Fiberall; Fibercon Caplets; Fiber-Lax; FiberNorm; Fleet Laxative; Fleet Mineral Oil; Fleet Phospho-Soda; Fleet Soflax Gelcaps; Fleet Soflax Overnight Gelcaps; Fletcher's Castoria; Genasoft Plus Softgels; Gentle Laxative; Haley's M-O; Herbal Laxative; Hydrocil Instant; Kondremul Plain; Konsyl; Konsyl Easy Mix; Konsyl-D; Konsyl-Orange; Konsyl-Orange Sugar Free; Laxinate 100; Liqui-Doss; Mag-Ox 400; Maltsupex; Metamucil; Metamucil Apple Crisp Fiber Wafers; Metamucil Cinnamon Spice Fiber Wafers; Metamucil Orange Flavor; Metamucil Smooth Sugar-Free, Citrus Flavor; Metamucil Smooth Sugar-Free, Orange Flavor; Metamucil Smooth Sugar-Free, Regular Flavor; Metamucil Smooth, Citrus Flavor; Metamucil Smooth, Orange Flavor; Metamucil Sugar-Free, Lemon-Lime

Flavor; Metamucil Sugar-Free, Orange Flavor; MiraLax; Modane; Modane Bulk; Mylanta Natural Fiber Supplement; Mylanta Sugar Free Natural Fiber Supplement; Nature's Remedy; Neoloid; Perdiem; Perdiem Fiber; Peri-Colace; Peri-Dos Softgels; Phillips' Chewable; Phillips' Concentrated; Phillips' Milk of Magnesia; Phillips' Stool Softner Laxative Softgels; Prompt; Purge; Reguloid Natural; Reguloid Natural Sugar Free; Reguloid Orange; Reguloid Orange Sugar Free; Senexon; Senna-Gen; Senokot; Senokot Children's Syrup; Senokot-S; SenokotXTRA; Senolax; Serutan; Serutan Toasted Granules; Silace; Silace-C; Sulfolax; Surfak; Syllact; Veracolate; V-Lax; X-Prep Liquid
http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202319.html

Niacin and Lovastatin

- **Systemic - U.S. Brands:** Advicor
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500381.html

Niacin For High Cholesterol

- **Systemic - U.S. Brands:** Niacor; Niaspan; Nicolar; Nicotinex Elixir; Slo-Niacin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202404.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.

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[10]:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://www.cancer.gov/cancerinfo/list.aspx?viewid=5f35036e-5497-4d86-8c2c-714a9f7c8d25**
- National Eye Institute (NEI); guidelines available at **http://www.nei.nih.gov/order/index.htm**
- National Heart, Lung, and Blood Institute (NHLBI); guidelines available at **http://www.nhlbi.nih.gov/guidelines/index.htm**
- National Human Genome Research Institute (NHGRI); research available at **http://www.genome.gov/page.cfm?pageID=10000375**
- National Institute on Aging (NIA); guidelines available at **http://www.nia.nih.gov/health/**

[10] These publications are typically written by one or more of the various NIH Institutes.

- National Institute on Alcohol Abuse and Alcoholism (NIAAA); guidelines available at **http://www.niaaa.nih.gov/publications/publications.htm**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); fact sheets and guidelines available at **http://www.niams.nih.gov/hi/index.htm**
- National Institute of Child Health and Human Development (NICHD); guidelines available at **http://www.nichd.nih.gov/publications/pubskey.cfm**
- National Institute on Deafness and Other Communication Disorders (NIDCD); fact sheets and guidelines at **http://www.nidcd.nih.gov/health/**
- National Institute of Dental and Craniofacial Research (NIDCR); guidelines available at **http://www.nidr.nih.gov/health/**
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); guidelines available at **http://www.niddk.nih.gov/health/health.htm**
- National Institute on Drug Abuse (NIDA); guidelines available at **http://www.nida.nih.gov/DrugAbuse.html**
- National Institute of Environmental Health Sciences (NIEHS); environmental health information available at **http://www.niehs.nih.gov/external/facts.htm**
- National Institute of Mental Health (NIMH); guidelines available at **http://www.nimh.nih.gov/practitioners/index.cfm**
- National Institute of Neurological Disorders and Stroke (NINDS); neurological disorder information pages available at **http://www.ninds.nih.gov/health_and_medical/disorder_index.htm**
- National Institute of Nursing Research (NINR); publications on selected illnesses at **http://www.nih.gov/ninr/news-info/publications.html**
- National Institute of Biomedical Imaging and Bioengineering; general information at **http://grants.nih.gov/grants/becon/becon_info.htm**
- Center for Information Technology (CIT); referrals to other agencies based on keyword searches available at **http://kb.nih.gov/www_query_main.asp**
- National Center for Complementary and Alternative Medicine (NCCAM); health information available at **http://nccam.nih.gov/health/**
- National Center for Research Resources (NCRR); various information directories available at **http://www.ncrr.nih.gov/publications.asp**
- Office of Rare Diseases; various fact sheets available at **http://rarediseases.info.nih.gov/html/resources/rep_pubs.html**
- Centers for Disease Control and Prevention; various fact sheets on infectious diseases available at **http://www.cdc.gov/publications.htm**

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[11] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full-text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[12]

- **Bioethics:** Access to published literature on the ethical, legal, and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to cancer-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**

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[11] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[12] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

The NLM Gateway[13]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface, providing one-stop searching for many of NLM's information resources or databases.[14] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "hyperlipidemia" (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	42103
Books / Periodicals / Audio Visual	326
Consumer Health	162
Meeting Abstracts	207
Other Collections	145
Total	42943

HSTAT[15]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[16] These documents include clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[17] Simply search by "hyperlipidemia" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

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

[14] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

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

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

[17] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services' *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.

Coffee Break: Tutorials for Biologists[18]

Coffee Break is a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. Here you will find a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[19] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[20] This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

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

[19] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[20] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

APPENDIX B. PATIENT RESOURCES

Overview

Official agencies, as well as federally funded institutions supported by national grants, frequently publish a variety of guidelines written with the patient in mind. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. Since new guidelines on hyperlipidemia 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 hyperlipidemia. 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 hyperlipidemia. 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 "hyperlipidemia":

African-American Health
http://www.nlm.nih.gov/medlineplus/africanamericanhealth.html

Diabetes
http://www.nlm.nih.gov/medlineplus/diabetes.html

Diabetic Diet
http://www.nlm.nih.gov/medlineplus/diabeticdiet.html

Dietary Fats
http://www.nlm.nih.gov/medlineplus/dietaryfats.html

Heart Diseases
http://www.nlm.nih.gov/medlineplus/heartdiseases.html

You may also choose to use the search utility provided by MEDLINEplus at the following Web address: **http://www.nlm.nih.gov/medlineplus/**. Simply type a keyword into the search box and click "Search." This utility is similar to the NIH search utility, with the exception that it only includes materials that are linked within the MEDLINEplus system (mostly patient-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The Combined Health Information Database (CHID)

CHID Online is a reference tool that maintains a database directory of thousands of journal articles and patient education guidelines on hyperlipidemia. 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:

- **IgA Nephropathy: Questions and Answers. A Guide for Parents**

  Source: Jenkintown, PA: IgA Nephropathy Support Network. 1996. 10 p.

  Contact: Available from IgA Nephropathy Support Network. 234 Summit Avenue, Jenkintown, PA 19046. (215) 884-9038. PRICE: Single copy free.
  Summary: This lengthy fact sheet provides information about IgA nephropathy, a type of glomerulonephritis (kidney infection). Written in a question-and-answer format, the fact sheet outlines the pathology of IgA nephropathy and then covers diagnosis and diagnostic tests, including the indications for kidney biopsy; the etiology of IgA nephropathy; and the incidence and prevalence of the disease. The author describes symptoms, including proteinuria, hematuria, and the development of the nephrotic syndrome; accompanying problems, including flank pain, hypertension, **hyperlipidemia,** mood swings, and exhaustion; the progression and prognosis of the disease; treatment options, including drug therapy with immunosuppressants and diet therapy; and what happens to patients who go on to kidney failure. The author encourages parents to arm themselves with information and to become an active member of their child's health care team. The fact sheet includes the address of the IgA Nephropathy Support Network.

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 hyperlipidemia. 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 hyperlipidemia. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with hyperlipidemia.

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 hyperlipidemia. 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 "hyperlipidemia" (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 "hyperlipidemia". 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 "hyperlipidemia" (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 "hyperlipidemia" (or a synonym) into the search box, and click "Submit Query."

APPENDIX C. FINDING MEDICAL LIBRARIES

Overview

In this Appendix, we show you how to quickly find a medical library in your area.

Preparation

Your local public library and medical libraries have interlibrary loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[21]

Finding a Local Medical Library

The quickest method to locate medical libraries is to use the Internet-based directory published by the National Network of Libraries of Medicine (NN/LM). This network includes 4626 members and affiliates that provide many services to librarians, health professionals, and the public. To find a library in your area, simply visit **http://nnlm.gov/members/adv.html** or call 1-800-338-7657.

Medical Libraries in the U.S. and Canada

In addition to the NN/LM, the National Library of Medicine (NLM) lists a number of libraries with reference facilities that are open to the public. The following is the NLM's list and includes hyperlinks to each library's Web site. These Web pages can provide information on hours of operation and other restrictions. The list below is a small sample of

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[21] Adapted from the NLM: **http://www.nlm.nih.gov/psd/cas/interlibrary.html**.

libraries recommended by the National Library of Medicine (sorted alphabetically by name of the U.S. state or Canadian province where the library is located)[22]:

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute)
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System, Humboldt), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos, **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**
- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** Los Gatos PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation, Sacramento), **http://suttermedicalcenter.org/library/**
- **California:** Health Sciences Libraries (University of California, Davis), **http://www.lib.ucdavis.edu/healthsci/**
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System, Pleasanton), **http://gaelnet.stmarys-ca.edu/other.libs/gbal/east/vchl.html**
- **California:** Washington Community Health Resource Library (Fremont), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.saintjosephdenver.org/yourhealth/libraries/**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**

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[22] Abstracted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital, Waterbury), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute, Wilmington), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine, Wilmington), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia, Augusta), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia, Macon), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library, Honolulu), **http://hml.org/CHIS/**
- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center, Coeur d'Alene), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Chicago), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center, Peoria), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital, Lexington), **http://www.centralbap.com/education/community/library.cfm**
- **Kentucky:** University of Kentucky - Health Information Library (Chandler Medical Center, Lexington), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation, New Orleans), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital, Farmington), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center, Lewiston), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare, Bangor), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center, Portland), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital (Brunswick), **http://www.parkviewhospital.org/**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center, Biddeford), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital's Health Information Library (Western Maine Health, Norway), **http://www.wmhcc.org/Library/**

- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre, Winnipeg), **http://www.deerlodge.mb.ca/crane_library/about.asp**
- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital, Lowell), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital, Boston), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital, Southcoast Health System, New Bedford), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School, Worchester), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center, Ann Arbor), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information (Detroit), **http://www.henryford.com/body.cfm?id=39330**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center, Missoula)
- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**

- **Nevada:** Health Science Library, West Charleston Library (Las Vegas-Clark County Library District, Las Vegas), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library, Hanover), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital, Rahway), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center, Englewood), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center, Englewood), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York, Syracuse), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center, New Hyde Park), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** The Health Information Center at Saint Francis Hospital (Saint Francis Health System, Tulsa), **http://www.sfh-tulsa.com/services/healthinfo.asp**
- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center, The Dalles), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center, Hershey), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center, Danville), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital, Scranton), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System, Pittsburgh), **http://www.hsls.pitt.edu/guides/chi/hopwood/index_html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System, Williamsport), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System, Pittsburgh), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://www.mghlib.mcgill.ca/**

- **South Dakota:** Rapid City Regional Hospital Medical Library (Rapid City Regional Hospital), **http://www.rcrh.org/Services/Library/Default.asp**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center, Vancouver), **http://www.swmedicalcenter.com/body.cfm?id=72**

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://cancerweb.ncl.ac.uk/omd/**
- Rare Diseases Terms (Office of Rare Diseases): **http://ord.aspensys.com/asp/diseases/diseases.asp**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**

Beyond these, MEDLINEplus contains a very patient-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia can be accessed at **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as drkoop.com (**http://www.drkoop.com/**) and Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a**). The NIH suggests the following Web sites in the ADAM Medical Encyclopedia when searching for information on hyperlipidemia:

- **Basic Guidelines for Hyperlipidemia**

  Hyperlipidemia - acquired
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000403.htm

- **Signs & Symptoms for Hyperlipidemia**

  Obesity
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003101.htm

  Overweight
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003101.htm

- **Diagnostics and Tests for Hyperlipidemia**

  HDL
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003496.htm

  LDL
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003495.htm

Triglycerides
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003493.htm

- **Nutrition for Hyperlipidemia**

Cholesterol
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002472.htm

Fat
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002468.htm

Lipids
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002468.htm

Protein
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002467.htm

Saturated fat
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002468.htm

- **Background Topics for Hyperlipidemia**

Cardiovascular
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002310.htm

Heart disease
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000147.htm

Ideal body weight
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001938.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

Weight reduction
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001940.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

HYPERLIPIDEMIA DICTIONARY

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

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 fat: Fat (adipose tissue) that is centrally distributed between the thorax and pelvis and that induces greater health risk. [NIH]

Abdominal Pain: Sensation of discomfort, distress, or agony in the abdominal region. [NIH]

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

Ablation: The removal of an organ by surgery. [NIH]

Acceptor: A substance which, while normally not oxidized by oxygen or reduced by hydrogen, can be oxidized or reduced in presence of a substance which is itself undergoing oxidation or reduction. [NIH]

Acculturation: Process of cultural change in which one group or members of a group assimilates various cultural patterns from another. [NIH]

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

Acetone: A colorless liquid used as a solvent and an antiseptic. It is one of the ketone bodies produced during ketoacidosis. [NIH]

Acetylcholine: A neurotransmitter. Acetylcholine in vertebrates is the major transmitter at neuromuscular junctions, autonomic ganglia, parasympathetic effector junctions, a subset of sympathetic effector junctions, and at many sites in the central nervous system. It is generally not used as an administered drug because it is broken down very rapidly by cholinesterases, but it is useful in some ophthalmological applications. [NIH]

Acidosis: A pathologic condition resulting from accumulation of acid or depletion of the alkaline reserve (bicarbonate content) in the blood and body tissues, and characterized by an increase in hydrogen ion concentration. [EU]

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

Acyl: Chemical signal used by bacteria to communicate. [NIH]

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

Adaptation: 1. The adjustment of an organism to its environment, or the process by which it enhances such fitness. 2. The normal ability of the eye to adjust itself to variations in the intensity of light; the adjustment to such variations. 3. The decline in the frequency of firing of a neuron, particularly of a receptor, under conditions of constant stimulation. 4. In dentistry, (a) the proper fitting of a denture, (b) the degree of proximity and interlocking of restorative material to a tooth preparation, (c) the exact adjustment of bands to teeth. 5. In microbiology, the adjustment of bacterial physiology to a new environment. [EU]

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]

Adenovirus: A group of viruses that cause respiratory tract and eye infections. Adenoviruses used in gene therapy are altered to carry a specific tumor-fighting gene. [NIH]

Adipocytes: Fat-storing cells found mostly in the abdominal cavity and subcutaneous tissue. Fat is usually stored in the form of tryglycerides. [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]

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

Adolescent Nutrition: Nutrition of children aged 13-18 years. [NIH]

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

Adrenaline: A hormone. Also called epinephrine. [NIH]

Adrenergic: Activated by, characteristic of, or secreting epinephrine or substances with similar activity; the term is applied to those nerve fibres that liberate norepinephrine at a synapse when a nerve impulse passes, i.e., the sympathetic fibres. [EU]

Adrenergic Agents: Drugs that act on adrenergic receptors or affect the life cycle of adrenergic transmitters. Included here are adrenergic agonists and antagonists and agents that affect the synthesis, storage, uptake, metabolism, or release of adrenergic transmitters. [NIH]

Adrenoreceptor: Receptors specifically sensitive to and operated by adrenaline and/or noradrenaline and related sympathomimetic drugs. Adrenoreceptor is an alternative name. [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]

Aerobic Exercise: A type of physical activity that includes walking, jogging, running, and dancing. Aerobic training improves the efficiency of the aerobic energy-producing systems that can improve cardiorespiratory endurance. [NIH]

Afferent: Concerned with the transmission of neural impulse toward the central part of the nervous system. [NIH]

Affinity: 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of

antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

Agar: A complex sulfated polymer of galactose units, extracted from Gelidium cartilagineum, Gracilaria confervoides, and related red algae. It is used as a gel in the preparation of solid culture media for microorganisms, as a bulk laxative, in making emulsions, and as a supporting medium for immunodiffusion and immunoelectrophoresis. [NIH]

Age Groups: Persons classified by age from birth (infant, newborn) to octogenarians and older (aged, 80 and over). [NIH]

Age of Onset: The age or period of life at which a disease or the initial symptoms or manifestations of a disease appear in an individual. [NIH]

Age-Adjusted: Summary measures of rates of morbidity or mortality in a population using statistical procedures to remove the effect of age differences in populations that are being compared. Age is probably the most important and the most common variable in determining the risk of morbidity and mortality. [NIH]

Aged, 80 and Over: A person 80 years of age and older. [NIH]

Agonist: In anatomy, a prime mover. In pharmacology, a drug that has affinity for and stimulates physiologic activity at cell receptors normally stimulated by naturally occurring substances. [EU]

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

Akathisia: 1. A condition of motor restlessness in which there is a feeling of muscular quivering, an urge to move about constantly, and an inability to sit still, a common extrapyramidal side effect of neuroleptic drugs. 2. An inability to sit down because of intense anxiety at the thought of doing so. [EU]

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]

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

Alkaloid: A member of a large group of chemicals that are made by plants and have nitrogen in them. Some alkaloids have been shown to work against cancer. [NIH]

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

Allergens: Antigen-type substances that produce immediate hypersensitivity (hypersensitivity, immediate). [NIH]

Allograft: An organ or tissue transplant between two humans. [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-fetoprotein: AFP. A protein normally produced by a developing fetus. AFP levels are usually undetectable in the blood of healthy nonpregnant adults. An elevated level of AFP suggests the presence of either a primary liver cancer or germ cell tumor. [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]

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

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

Amino acid: Any organic compound containing an amino (-NH2 and a carboxyl (- COOH) group. The 20 a-amino acids listed in the accompanying table are the amino acids from which proteins are synthesized by formation of peptide bonds during ribosomal translation of messenger RNA; all except glycine, which is not optically active, have the L configuration. Other amino acids occurring in proteins, such as hydroxyproline in collagen, are formed by posttranslational enzymatic modification of amino acids residues in polypeptide chains. There are also several important amino acids, such as the neurotransmitter y-aminobutyric acid, that have no relation to proteins. Abbreviated AA. [EU]

Amino-terminal: The end of a protein or polypeptide chain that contains a free amino group (-NH2). [NIH]

Amlodipine: 2-((2-Aminoethoxy)methyl)-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylic acid 3-ethyl 5-methyl ester. A long-acting dihydropyridine calcium channel blocker. It is effective in the treatment of angina pectoris and hypertension. [NIH]

Amnestic: Nominal aphasia; a difficulty in finding the right name for an object. [NIH]

Amphetamines: Analogs or derivatives of amphetamine. Many are sympathomimetics and central nervous system stimulators causing excitation, vasopression, bronchodilation, and to varying degrees, anorexia, analepsis, nasal decongestion, and some smooth muscle relaxation. [NIH]

Anabolic: Relating to, characterized by, or promoting anabolism. [EU]

Anaerobic: 1. Lacking molecular oxygen. 2. Growing, living, or occurring in the absence of molecular oxygen; pertaining to an anaerobe. [EU]

Anaesthesia: Loss of feeling or sensation. Although the term is used for loss of tactile sensibility, or of any of the other senses, it is applied especially to loss of the sensation of pain, as it is induced to permit performance of surgery or other painful procedures. [EU]

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

Analog: In chemistry, a substance that is similar, but not identical, to another. [NIH]

Analogous: Resembling or similar in some respects, as in function or appearance, but not in origin or development;. [EU]

Analytes: A component of a test sample the presence of which has to be demonstrated. The

term "analyte" includes where appropriate formed from the analyte during the analyses. [NIH]

Anaphylatoxins: The family of peptides C3a, C4a, C5a, and C5a des-arginine produced in the serum during complement activation. They produce smooth muscle contraction, mast cell histamine release, affect platelet aggregation, and act as mediators of the local inflammatory process. The order of anaphylatoxin activity from strongest to weakest is C5a, C3a, C4a, and C5a des-arginine. The latter is the so-called "classical" anaphylatoxin but shows no spasmogenic activity though it contains some chemotactic ability. [NIH]

Anastomosis: A procedure to connect healthy sections of tubular structures in the body after the diseased portion has been surgically removed. [NIH]

Anatomical: Pertaining to anatomy, or to the structure of the organism. [EU]

Androgenic: Producing masculine characteristics. [EU]

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

Androstenedione: A steroid with androgenic properties that is produced in the testis, ovary, and adrenal cortex. It is a precursor to testosterone and other androgenic hormones. [NIH]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

Anesthesia: A state characterized by loss of feeling or sensation. This depression of nerve function is usually the result of pharmacologic action and is induced to allow performance of surgery or other painful procedures. [NIH]

Aneurysm: A sac formed by the dilatation of the wall of an artery, a vein, or the heart. [NIH]

Angina: Chest pain that originates in the heart. [NIH]

Angina Pectoris: The symptom of paroxysmal pain consequent to myocardial ischemia usually of distinctive character, location and radiation, and provoked by a transient stressful situation during which the oxygen requirements of the myocardium exceed the capacity of the coronary circulation to supply it. [NIH]

Angiogenesis: Blood vessel formation. Tumor angiogenesis is the growth of blood vessels from surrounding tissue to a solid tumor. This is caused by the release of chemicals by the tumor. [NIH]

Angiotensin I: The decapeptide precursor of angiotensin II, generated by the action of renin on angiotensinogen. It has limited pharmacologic activity. [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]

Anhydrous: Deprived or destitute of water. [EU]

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]

Anode: Electrode held at a positive potential with respect to a cathode. [NIH]

Antagonism: Interference with, or inhibition of, the growth of a living organism by another

living organism, due either to creation of unfavorable conditions (e. g. exhaustion of food supplies) or to production of a specific antibiotic substance (e. g. penicillin). [NIH]

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]

Antidiabetic: An agent that prevents or alleviates diabetes. [EU]

Antidiabetic Agent: A substance that helps a person with diabetes control the level of glucose (sugar) in the blood so that the body works as it should. [NIH]

Antiemetic: An agent that prevents or alleviates nausea and vomiting. Also antinauseant. [EU]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Antigen-Antibody Complex: The complex formed by the binding of antigen and antibody molecules. The deposition of large antigen-antibody complexes leading to tissue damage causes immune complex diseases. [NIH]

Anti-infective: An agent that so acts. [EU]

Anti-Infective Agents: Substances that prevent infectious agents or organisms from spreading or kill infectious agents in order to prevent the spread of infection. [NIH]

Anti-inflammatory: Having to do with reducing inflammation. [NIH]

Antioxidant: A substance that prevents damage caused by free radicals. Free radicals are highly reactive chemicals that often contain oxygen. They are produced when molecules are split to give products that have unpaired electrons. This process is called oxidation. [NIH]

Antipruritic: Relieving or preventing itching. [EU]

Antipsychotic: Effective in the treatment of psychosis. Antipsychotic drugs (called also neuroleptic drugs and major tranquilizers) are a chemically diverse (including phenothiazines, thioxanthenes, butyrophenones, dibenzoxazepines, dibenzodiazepines, and diphenylbutylpiperidines) but pharmacologically similar class of drugs used to treat schizophrenic, paranoid, schizoaffective, and other psychotic disorders; acute delirium and dementia, and manic episodes (during induction of lithium therapy); to control the movement disorders associated with Huntington's chorea, Gilles de la Tourette's syndrome, and ballismus; and to treat intractable hiccups and severe nausea and vomiting. Antipsychotic agents bind to dopamine, histamine, muscarinic cholinergic, a-adrenergic, and serotonin receptors. Blockade of dopaminergic transmission in various areas is thought

to be responsible for their major effects : antipsychotic action by blockade in the mesolimbic and mesocortical areas; extrapyramidal side effects (dystonia, akathisia, parkinsonism, and tardive dyskinesia) by blockade in the basal ganglia; and antiemetic effects by blockade in the chemoreceptor trigger zone of the medulla. Sedation and autonomic side effects (orthostatic hypotension, blurred vision, dry mouth, nasal congestion and constipation) are caused by blockade of histamine, cholinergic, and adrenergic receptors. [EU]

Antiseptic: A substance that inhibits the growth and development of microorganisms without necessarily killing them. [EU]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Antiviral Agents: Agents used in the prophylaxis or therapy of virus diseases. Some of the ways they may act include preventing viral replication by inhibiting viral DNA polymerase; binding to specific cell-surface receptors and inhibiting viral penetration or uncoating; inhibiting viral protein synthesis; or blocking late stages of virus assembly. [NIH]

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

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

Anxiolytic: An anxiolytic or antianxiety agent. [EU]

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

Aortic Aneurysm: Aneurysm of the aorta. [NIH]

Aortic Valve: The valve between the left ventricle and the ascending aorta which prevents backflow into the left ventricle. [NIH]

Apheresis: Components being separated out, as leukapheresis, plasmapheresis, plateletpheresis. [NIH]

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

Apolipoproteins: The protein components of lipoproteins which remain after the lipids to which the proteins are bound have been removed. They play an important role in lipid transport and metabolism. [NIH]

Apolipoproteins A: Lipoproteins found in human blood serum in the high-density and very-high-density lipoprotein fraction (HDL, VHDL). They consist of several different polypeptides, the most important of which are apolipoprotein A-I and A-II. They maintain the structural integrity of the HDL particles and are activators of lecithin:cholesterol acyltransferase (LCAT). Atherosclerotic patients show low apolipoprotein A levels and these apolipoproteins are either absent or present in extremely low plasma concentration in Tangier disease. [NIH]

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

Aqueous: Having to do with water. [NIH]

Arachidonic Acid: An unsaturated, essential fatty acid. It is found in animal and human fat as well as in the liver, brain, and glandular organs, and is a constituent of animal phosphatides. It is formed by the synthesis from dietary linoleic acid and is a precursor in the biosynthesis of prostaglandins, thromboxanes, and leukotrienes. [NIH]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Arteriolosclerosis: Sclerosis and thickening of the walls of the smaller arteries (arterioles). Hyaline arteriolosclerosis, in which there is homogeneous pink hyaline thickening of the arteriolar walls, is associated with benign nephrosclerosis. Hyperplastic arteriolosclerosis, in which there is a concentric thickening with progressive narrowing of the lumina may be associated with malignant hypertension, nephrosclerosis, and scleroderma. [EU]

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

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

Artery: Vessel-carrying blood from the heart to various parts of the body. [NIH]

Articular: Of or pertaining to a joint. [EU]

Aspartic: The naturally occurring substance is L-aspartic acid. One of the acidic-amino-acids is obtained by the hydrolysis of proteins. [NIH]

Aspartic Endopeptidases: A sub-subclass of endopeptidases that depend on an aspartic acid residue for their activity. EC 3.4.23. [NIH]

Aspiration: The act of inhaling. [NIH]

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

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Atenolol: A cardioselective beta-adrenergic blocker possessing properties and potency similar to propranolol, but without a negative inotropic effect. [NIH]

Atherogenic: Causing the formation of plaque in the lining of the arteries. [NIH]

Atheromatosis: A diffuse atheromatous disease of the arteries. [EU]

Atresia: Lack of a normal opening from the esophagus, intestines, or anus. [NIH]

Atrophy: Decrease in the size of a cell, tissue, organ, or multiple organs, associated with a variety of pathological conditions such as abnormal cellular changes, ischemia, malnutrition, or hormonal changes. [NIH]

Attenuated: Strain with weakened or reduced virulence. [NIH]

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

Autodigestion: Autolysis; a condition found in disease of the stomach: the stomach wall is digested by the gastric juice. [NIH]

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]

Autonomic: Self-controlling; functionally independent. [EU]

Autonomic Neuropathy: A disease of the nerves affecting mostly the internal organs such as the bladder muscles, the cardiovascular system, the digestive tract, and the genital organs. These nerves are not under a person's conscious control and function automatically. Also called visceral neuropathy. [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]

Axillary: Pertaining to the armpit area, including the lymph nodes that are located there. [NIH]

Axillary Artery: The continuation of the subclavian artery; it distributes over the upper limb, axilla, chest and shoulder. [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 Physiology: Physiological processes and activities of bacteria. [NIH]

Bactericidal: Substance lethal to bacteria; substance capable of killing bacteria. [NIH]

Bacteriophage: A virus whose host is a bacterial cell; A virus that exclusively infects bacteria. It generally has a protein coat surrounding the genome (DNA or RNA). One of the coliphages most extensively studied is the lambda phage, which is also one of the most important. [NIH]

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

Basal Ganglia: Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [NIH]

Basement Membrane: Ubiquitous supportive tissue adjacent to epithelium and around smooth and striated muscle cells. This tissue contains intrinsic macromolecular components such as collagen, laminin, and sulfated proteoglycans. As seen by light microscopy one of its subdivisions is the basal (basement) lamina. [NIH]

Basophils: Granular leukocytes characterized by a relatively pale-staining, lobate nucleus and cytoplasm containing coarse dark-staining granules of variable size and stainable by basic dyes. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Benzene: Toxic, volatile, flammable liquid hydrocarbon biproduct of coal distillation. It is used as an industrial solvent in paints, varnishes, lacquer thinners, gasoline, etc. Benzene causes central nervous system damage acutely and bone marrow damage chronically and is carcinogenic. It was formerly used as parasiticide. [NIH]

Bezafibrate: Antilipemic agent that lowers cholesterol and triglycerides. It decreases low density lipoproteins and increases high density lipoproteins. [NIH]

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

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

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

Bile Acids and Salts: Steroid acids and salts. The primary bile acids are derived from cholesterol in the liver and usually conjugated with glycine or taurine. The secondary bile acids are further modified by bacteria in the intestine. They play an important role in the digestion and absorption of fat. They have also been used pharmacologically, especially in the treatment of gallstones. [NIH]

Bile duct: A tube through which bile passes in and out of the liver. [NIH]

Biliary: Having to do with the liver, bile ducts, and/or gallbladder. [NIH]

Biliary Tract: The gallbladder and its ducts. [NIH]

Bilirubin: A bile pigment that is a degradation product of heme. [NIH]

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

Bioavailability: The degree to which a drug or other substance becomes available to the target tissue after administration. [EU]

Bioavailable: The ability of a drug or other substance to be absorbed and used by the body. Orally bioavailable means that a drug or other substance that is taken by mouth can be absorbed and used by the body. [NIH]

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

Biological therapy: Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier (BRM) therapy. [NIH]

Biomolecular: A scientific field at the interface between advanced computing and biotechnology. [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]

Biotransformation: The chemical alteration of an exogenous substance by or in a biological system. The alteration may inactivate the compound or it may result in the production of an active metabolite of an inactive parent compound. The alteration may be either non-synthetic (oxidation-reduction, hydrolysis) or synthetic (glucuronide formation, sulfate conjugation, acetylation, methylation). This also includes metabolic detoxication and clearance. [NIH]

Bladder: The organ that stores urine. [NIH]

Blast phase: The phase of chronic myelogenous leukemia in which the number of immature, abnormal white blood cells in the bone marrow and blood is extremely high. Also called blast crisis. [NIH]

Blastocyst: The mammalian embryo in the post-morula stage in which a fluid-filled cavity,

enclosed primarily by trophoblast, contains an inner cell mass which becomes the embryonic disc. [NIH]

Bloating: Fullness or swelling in the abdomen that often occurs after meals. [NIH]

Blood Cell Count: A count of the number of leukocytes and erythrocytes per unit volume in a sample of venous blood. A complete blood count (CBC) also includes measurement of the hemoglobin, hematocrit, and erythrocyte indices. [NIH]

Blood Coagulation: The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [NIH]

Blood Glucose: Glucose in blood. [NIH]

Blood Platelets: Non-nucleated disk-shaped cells formed in the megakaryocyte and found in the blood of all mammals. They are mainly involved in blood coagulation. [NIH]

Blood pressure: The pressure of blood against the walls of a blood vessel or heart chamber. Unless there is reference to another location, such as the pulmonary artery or one of the heart chambers, it refers to the pressure in the systemic arteries, as measured, for example, in the forearm. [NIH]

Blood vessel: A tube in the body through which blood circulates. Blood vessels include a network of arteries, arterioles, capillaries, venules, and veins. [NIH]

Blood-Brain Barrier: Specialized non-fenestrated tightly-joined endothelial cells (tight junctions) that form a transport barrier for certain substances between the cerebral capillaries and the brain tissue. [NIH]

Blot: To transfer DNA, RNA, or proteins to an immobilizing matrix such as nitrocellulose. [NIH]

Body Composition: The relative amounts of various components in the body, such as percent body fat. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Body Mass Index: One of the anthropometric measures of body mass; it has the highest correlation with skinfold thickness or body density. [NIH]

Body Weight Changes: A clinical manifestation consisting of alterations in an individual's weight from his or her norm. [NIH]

Bone Density: The amount of mineral per square centimeter of bone. This is the definition used in clinical practice. Actual bone density would be expressed in grams per milliliter. It is most frequently measured by photon absorptiometry or x-ray computed tomography. [NIH]

Bone Marrow: The soft tissue filling the cavities of bones. Bone marrow exists in two types, yellow and red. Yellow marrow is found in the large cavities of large bones and consists mostly of fat cells and a few primitive blood cells. Red marrow is a hematopoietic tissue and is the site of production of erythrocytes and granular leukocytes. Bone marrow is made up of a framework of connective tissue containing branching fibers with the frame being filled with marrow cells. [NIH]

Bone Marrow Cells: Cells contained in the bone marrow including fat cells, stromal cells, megakaryocytes, and the immediate precursors of most blood cells. [NIH]

Bone Marrow Transplantation: The transference of bone marrow from one human or animal to another. [NIH]

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]

Boron: A trace element with the atomic symbol B, atomic number 5, and atomic weight

10.81. Boron-10, an isotope of boron, is used as a neutron absorber in boron neutron capture therapy. [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]

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

Brachial Artery: The continuation of the axillary artery; it branches into the radial and ulnar arteries. [NIH]

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]

Bronchoconstriction: Diminution of the caliber of a bronchus physiologically or as a result of pharmacological intervention. [NIH]

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

Caecum: The blind pouch in which the large intestine begins and into which the ileum opens from one side. [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]

Calcineurin: A calcium- and calmodulin-binding protein present in highest concentrations in the central nervous system. Calcineurin is composed of two subunits. A catalytic subunit, calcineurin A, and a regulatory subunit, calcineurin B, with molecular weights of about 60 kD and 19 kD, respectively. Calcineurin has been shown to dephosphorylate a number of phosphoproteins including histones, myosin light chain, and the regulatory subunit of cAMP-dependent protein kinase. It is involved in the regulation of signal transduction and is the target of an important class of immunophilin-immunosuppressive drug complexes in T-lymphocytes that act by inhibiting T-cell activation. EC 3.1.3.-. [NIH]

Calcium: A basic element found in nearly all organized tissues. It is a member of the alkaline earth family of metals with the atomic symbol Ca, atomic number 20, and atomic weight 40. Calcium is the most abundant mineral in the body and combines with phosphorus to form calcium phosphate in the bones and teeth. It is essential for the normal functioning of nerves and muscles and plays a role in blood coagulation (as factor IV) and in many enzymatic processes. [NIH]

Calcium channel blocker: A drug used to relax the blood vessel and heart muscle, causing pressure inside blood vessels to drop. It also can regulate heart rhythm. [NIH]

Calmodulin: A heat-stable, low-molecular-weight activator protein found mainly in the brain and heart. The binding of calcium ions to this protein allows this protein to bind to cyclic nucleotide phosphodiesterases and to adenyl cyclase with subsequent activation. Thereby this protein modulates cyclic AMP and cyclic GMP levels. [NIH]

Capillary: Any one of the minute vessels that connect the arterioles and venules, forming a network in nearly all parts of the body. Their walls act as semipermeable membranes for the interchange of various substances, including fluids, between the blood and tissue fluid; called also vas capillare. [EU]

Capillary Fragility: The lack of resistance, or susceptibility, of capillaries to damage or disruption under conditions of increased stress. [NIH]

Capsules: Hard or soft soluble containers used for the oral administration of medicine. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH2O)n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carbon Dioxide: A colorless, odorless gas that can be formed by the body and is necessary for the respiration cycle of plants and animals. [NIH]

Carboxy: Cannabinoid. [NIH]

Carboxylic Acids: Organic compounds containing the carboxy group (-COOH). This group of compounds includes amino acids and fatty acids. Carboxylic acids can be saturated, unsaturated, or aromatic. [NIH]

Carcinogen: Any substance that causes cancer. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Carcinoma: Cancer that begins in the skin or in tissues that line or cover internal organs. [NIH]

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

Cardiomyopathy: A general diagnostic term designating primary myocardial disease, often of obscure or unknown etiology. [EU]

Cardiorespiratory: Relating to the heart and lungs and their function. [EU]

Cardioselective: Having greater activity on heart tissue than on other tissue. [EU]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular disease: Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

Cardiovascular System: The heart and the blood vessels by which blood is pumped and circulated through the body. [NIH]

Carnitine: Constituent of striated muscle and liver. It is used therapeutically to stimulate gastric and pancreatic secretions and in the treatment of hyperlipoproteinemias. [NIH]

Carrier State: The condition of harboring an infective organism without manifesting symptoms of infection. The organism must be readily transmissable to another susceptible host. [NIH]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

Case-Control Studies: Studies which start with the identification of persons with a disease of interest and a control (comparison, referent) group without the disease. The relationship of an attribute to the disease is examined by comparing diseased and non-diseased persons

with regard to the frequency or levels of the attribute in each group. [NIH]

Castration: Surgical removal or artificial destruction of gonads. [NIH]

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

Catecholamine: A group of chemical substances manufactured by the adrenal medulla and secreted during physiological stress. [NIH]

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

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [NIH]

Cecum: The beginning of the large intestine. The cecum is connected to the lower part of the small intestine, called the ileum. [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 Adhesion: Adherence of cells to surfaces or to other cells. [NIH]

Cell Adhesion Molecules: Surface ligands, usually glycoproteins, that mediate cell-to-cell adhesion. Their functions include the assembly and interconnection of various vertebrate systems, as well as maintenance of tissue integration, wound healing, morphogenic movements, cellular migrations, and metastasis. [NIH]

Cell Aggregation: The phenomenon by which dissociated cells intermixed in vitro tend to group themselves with cells of their own type. [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 Division: The fission of a cell. [NIH]

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

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

Cell Respiration: The metabolic process of all living cells (animal and plant) in which oxygen is used to provide a source of energy for the cell. [NIH]

Cell Size: The physical dimensions of a cell. It refers mainly to changes in dimensions correlated with physiological or pathological changes in cells. [NIH]

Cell 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]

Cellular metabolism: The sum of all chemical changes that take place in a cell through which energy and basic components are provided for essential processes, including the synthesis of new molecules and the breakdown and removal of others. [NIH]

Cellulose: A polysaccharide with glucose units linked as in cellobiose. It is the chief constituent of plant fibers, cotton being the purest natural form of the substance. As a raw material, it forms the basis for many derivatives used in chromatography, ion exchange

materials, explosives manufacturing, and pharmaceutical preparations. [NIH]

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

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

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]

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

Cerebral Angiography: Radiography of the vascular system of the brain after injection of a contrast medium. [NIH]

Cerebral Cortex: The thin layer of gray matter on the surface of the cerebral hemisphere that develops from the telencephalon and folds into gyri. It reaches its highest development in man and is responsible for intellectual faculties and higher mental functions. [NIH]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

Character: In current usage, approximately equivalent to personality. The sum of the relatively fixed personality traits and habitual modes of response of an individual. [NIH]

Chemokines: Class of pro-inflammatory cytokines that have the ability to attract and activate leukocytes. They can be divided into at least three structural branches: C (chemokines, C), CC (chemokines, CC), and CXC (chemokines, CXC), according to variations in a shared cysteine motif. [NIH]

Chemoreceptor: A receptor adapted for excitation by chemical substances, e.g., olfactory and gustatory receptors, or a sense organ, as the carotid body or the aortic (supracardial) bodies, which is sensitive to chemical changes in the blood stream, especially reduced oxygen content, and reflexly increases both respiration and blood pressure. [EU]

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]

Chemotaxis: The movement of cells or organisms toward or away from a substance in response to its concentration gradient. [NIH]

Chest Pain: Pressure, burning, or numbness in the chest. [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]

Cholesterol Esters: Fatty acid esters of cholesterol which constitute about two-thirds of the cholesterol in the plasma. The accumulation of cholesterol esters in the arterial intima is a characteristic feature of atherosclerosis. [NIH]

Cholestyramine: Strongly basic anion exchange resin whose main constituent is polystyrene trimethylbenzylammonium as Cl(-) anion. It exchanges chloride ions with bile salts, thus decreasing their concentration and that of cholesterol. It is used as a hypocholesteremic in

diarrhea and biliary obstruction and as an antipruritic. [NIH]

Choline: A basic constituent of lecithin that is found in many plants and animal organs. It is important as a precursor of acetylcholine, as a methyl donor in various metabolic processes, and in lipid metabolism. [NIH]

Cholinergic: Resembling acetylcholine in pharmacological action; stimulated by or releasing acetylcholine or a related compound. [EU]

Chondrocytes: Polymorphic cells that form cartilage. [NIH]

Chorea: Involuntary, forcible, rapid, jerky movements that may be subtle or become confluent, markedly altering normal patterns of movement. Hypotonia and pendular reflexes are often associated. Conditions which feature recurrent or persistent episodes of chorea as a primary manifestation of disease are referred to as choreatic disorders. Chorea is also a frequent manifestation of basal ganglia diseases. [NIH]

Chromaffin System: The cells of the body which stain with chromium salts. They occur along the sympathetic nerves, in the adrenal gland, and in various other organs. [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]

Chromium: A trace element that plays a role in glucose metabolism. It has the atomic symbol Cr, atomic number 24, and atomic weight 52. According to the Fourth Annual Report on Carcinogens (NTP85-002,1985), chromium and some of its compounds have been listed as known carcinogens. [NIH]

Chromosomal: Pertaining to chromosomes. [EU]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

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

Chronic Disease: Disease or ailment of long duration. [NIH]

Chronic lymphocytic leukemia: A slowly progressing disease in which too many white blood cells (called lymphocytes) are found in the body. [NIH]

Chronic myelogenous leukemia: CML. A slowly progressing disease in which too many white blood cells are made in the bone marrow. Also called chronic myeloid leukemia or chronic granulocytic leukemia. [NIH]

Chronic phase: Refers to the early stages of chronic myelogenous leukemia or chronic lymphocytic leukemia. The number of mature and immature abnormal white blood cells in the bone marrow and blood is higher than normal, but lower than in the accelerated or blast phase. [NIH]

Chronic renal: Slow and progressive loss of kidney function over several years, often resulting in end-stage renal disease. People with end-stage renal disease need dialysis or transplantation to replace the work of the kidneys. [NIH]

Chylomicrons: A class of lipoproteins that carry dietary cholesterol and triglycerides from the small intestines to the tissues. [NIH]

Circadian: Repeated more or less daily, i. e. on a 23- to 25-hour cycle. [NIH]

Circadian Rhythm: The regular recurrence, in cycles of about 24 hours, of biological processes or activities, such as sensitivity to drugs and stimuli, hormone secretion, sleeping, feeding, etc. This rhythm seems to be set by a 'biological clock' which seems to be set by recurring daylight and darkness. [NIH]

Circulatory system: The system that contains the heart and the blood vessels and moves blood throughout the body. This system helps tissues get enough oxygen and nutrients, and

it helps them get rid of waste products. The lymph system, which connects with the blood system, is often considered part of the circulatory system. [NIH]

Cirrhosis: A type of chronic, progressive liver disease. [NIH]

Clamp: A u-shaped steel rod used with a pin or wire for skeletal traction in the treatment of certain fractures. [NIH]

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

Clinical study: A research study in which patients receive treatment in a clinic or other medical facility. Reports of clinical studies can contain results for single patients (case reports) or many patients (case series or clinical trials). [NIH]

Clinical trial: A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

Clone: The term "clone" has acquired a new meaning. It is applied specifically to the bits of inserted foreign DNA in the hybrid molecules of the population. Each inserted segment originally resided in the DNA of a complex genome amid millions of other DNA segment. [NIH]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Clostridium: A genus of motile or nonmotile gram-positive bacteria of the family Bacillaceae. Many species have been identified with some being pathogenic. They occur in water, soil, and in the intestinal tract of humans and lower animals. [NIH]

Clostridium difficile: A common inhabitant of the colon flora in human infants and sometimes in adults. It produces a toxin that causes pseudomembranous enterocolitis in patients receiving antibiotic therapy. [NIH]

Clot Retraction: Retraction of a clot resulting from contraction of platelet pseudopods attached to fibrin strands that is dependent on the contractile protein thrombosthenin. Used as a measure of platelet function. [NIH]

Coca: Any of several South American shrubs of the Erythroxylon genus (and family) that yield cocaine; the leaves are chewed with alum for CNS stimulation. [NIH]

Cocaine: An alkaloid ester extracted from the leaves of plants including coca. It is a local anesthetic and vasoconstrictor and is clinically used for that purpose, particularly in the eye, ear, nose, and throat. It also has powerful central nervous system effects similar to the amphetamines and is a drug of abuse. Cocaine, like amphetamines, acts by multiple mechanisms on brain catecholaminergic neurons; the mechanism of its reinforcing effects is thought to involve inhibition of dopamine uptake. [NIH]

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]

Colestipol: Highly crosslinked and insoluble basic anion exchange resin used as anticholesteremic. It may also may reduce triglyceride levels. [NIH]

Colitis: Inflammation of the colon. [NIH]

Collagen: A polypeptide substance comprising about one third of the total protein in mammalian organisms. It is the main constituent of skin, connective tissue, and the organic

substance of bones and teeth. Different forms of collagen are produced in the body but all consist of three alpha-polypeptide chains arranged in a triple helix. Collagen is differentiated from other fibrous proteins, such as elastin, by the content of proline, hydroxyproline, and hydroxylysine; by the absence of tryptophan; and particularly by the high content of polar groups which are responsible for its swelling properties. [NIH]

Collagenous Colitis: A type of colitis. Caused by an abnormal band of collagen, a thread-like protein. [NIH]

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

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

Colon: The long, coiled, tubelike organ that removes water from digested food. The remaining material, solid waste called stool, moves through the colon to the rectum and leaves the body through the anus. [NIH]

Colon Polyps: Small, fleshy, mushroom-shaped growths in the colon. [NIH]

Common Bile Duct: The largest biliary duct. It is formed by the junction of the cystic duct and the hepatic duct. [NIH]

Comorbidity: The presence of co-existing or additional diseases with reference to an initial diagnosis or with reference to the index condition that is the subject of study. Comorbidity may affect the ability of affected individuals to function and also their survival; it may be used as a prognostic indicator for length of hospital stay, cost factors, and outcome or survival. [NIH]

Complement: A term originally used to refer to the heat-labile factor in serum that causes immune cytolysis, the lysis of antibody-coated cells, and now referring to the entire functionally related system comprising at least 20 distinct serum proteins that is the effector not only of immune cytolysis but also of other biologic functions. Complement activation occurs by two different sequences, the classic and alternative pathways. The proteins of the classic pathway are termed 'components of complement' and are designated by the symbols C1 through C9. C1 is a calcium-dependent complex of three distinct proteins C1q, C1r and C1s. The proteins of the alternative pathway (collectively referred to as the properdin system) and complement regulatory proteins are known by semisystematic or trivial names. Fragments resulting from proteolytic cleavage of complement proteins are designated with lower-case letter suffixes, e.g., C3a. Inactivated fragments may be designated with the suffix 'i', e.g. C3bi. Activated components or complexes with biological activity are designated by a bar over the symbol e.g. C1 or C4b,2a. The classic pathway is activated by the binding of C1 to classic pathway activators, primarily antigen-antibody complexes containing IgM, IgG1, IgG3; C1q binds to a single IgM molecule or two adjacent IgG molecules. The alternative pathway can be activated by IgA immune complexes and also by nonimmunologic materials including bacterial endotoxins, microbial polysaccharides, and cell walls. Activation of the classic pathway triggers an enzymatic cascade involving C1, C4, C2 and C3; activation of the alternative pathway triggers a cascade involving C3 and factors B, D and P. Both result in the cleavage of C5 and the formation of the membrane attack complex. Complement activation also results in the formation of many biologically active complement fragments that act as anaphylatoxins, opsonins, or chemotactic factors. [EU]

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]

Conception: The onset of pregnancy, marked by implantation of the blastocyst; the formation of a viable zygote. [EU]

Concomitant: Accompanying; accessory; joined with another. [EU]

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

Confusion: A mental state characterized by bewilderment, emotional disturbance, lack of clear thinking, and perceptual disorientation. [NIH]

Congestion: Excessive or abnormal accumulation of blood in a part. [EU]

Congestive heart failure: Weakness of the heart muscle that leads to a buildup of fluid in body tissues. [NIH]

Conjugated: Acting or operating as if joined; simultaneous. [EU]

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]

Constipation: Infrequent or difficult evacuation of feces. [NIH]

Constriction: The act of constricting. [NIH]

Contamination: The soiling or pollution by inferior material, as by the introduction of organisms into a wound, or sewage into a stream. [EU]

Contraception: Use of agents, devices, methods, or procedures which diminish the likelihood of or prevent conception. [NIH]

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]

Contrast Media: Substances used in radiography that allow visualization of certain tissues.

[NIH]

Control group: In a clinical trial, the group that does not receive the new treatment being studied. This group is compared to the group that receives the new treatment, to see if the new treatment works. [NIH]

Controlled clinical trial: A clinical study that includes a comparison (control) group. The comparison group receives a placebo, another treatment, or no treatment at all. [NIH]

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

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Coronary Arteriosclerosis: Thickening and loss of elasticity of the coronary arteries. [NIH]

Coronary Circulation: The circulation of blood through the coronary vessels of the heart. [NIH]

Coronary heart disease: A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

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

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

Cortisol: A steroid hormone secreted by the adrenal cortex as part of the body's response to stress. [NIH]

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

Cost-benefit: A quantitative technique of economic analysis which, when applied to radiation practice, compares the health detriment from the radiation doses concerned with the cost of radiation dose reduction in that practice. [NIH]

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

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

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]

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

Curcumin: A dye obtained from tumeric, the powdered root of Curcuma longa Linn. It is used in the preparation of curcuma paper and the detection of boron. Curcumin appears to possess a spectrum of pharmacological properties, due primarily to its inhibitory effects on metabolic enzymes. [NIH]

Cutaneous: Having to do with the skin. [NIH]

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

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

Cyclosporine: A drug used to help reduce the risk of rejection of organ and bone marrow transplants by the body. It is also used in clinical trials to make cancer cells more sensitive to anticancer drugs. [NIH]

Cystathionine beta-Synthase: A multifunctional pyridoxal phosphate enzyme. In the second stage of cysteine biosynthesis it catalyzes the reaction of homocysteine with serine to form cystathionine with the elimination of water. Deficiency of this enzyme leads to hyperhomocysteinemia and homocystinuria. EC 4.2.1.22. [NIH]

Cysteine: A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

Cysteine Endopeptidases: Endopeptidases which have a cysteine involved in the catalytic process. This group of enzymes is inactivated by sulfhydryl reagents. EC 3.4.22. [NIH]

Cystine: A covalently linked dimeric nonessential amino acid formed by the oxidation of cysteine. Two molecules of cysteine are joined together by a disulfide bridge to form cystine. [NIH]

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]

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

Cytotoxicity: Quality of being capable of producing a specific toxic action upon cells of special organs. [NIH]

Dairy Products: Raw and processed or manufactured milk and milk-derived products. These are usually from cows (bovine) but are also from goats, sheep, reindeer, and water buffalo. [NIH]

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

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

Decompensation: Failure of compensation; cardiac decompensation is marked by dyspnea, venous engorgement, and edema. [EU]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Dehydroepiandrosterone: DHEA. A substance that is being studied as a cancer prevention drug. It belongs to the family of drugs called steroids. [NIH]

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

Delirium: (DSM III-R) an acute, reversible organic mental disorder characterized by reduced ability to maintain attention to external stimuli and disorganized thinking as manifested by rambling, irrelevant, or incoherent speech; there are also a reduced level of consciousness, sensory misperceptions, disturbance of the sleep-wakefulness cycle and level of psychomotor activity, disorientation to time, place, or person, and memory impairment. Delirium may be caused by a large number of conditions resulting in derangement of

cerebral metabolism, including systemic infection, poisoning, drug intoxication or withdrawal, seizures or head trauma, and metabolic disturbances such as hypoxia, hypoglycaemia, fluid, electrolyte, or acid-base imbalances, or hepatic or renal failure. Called also acute confusional state and acute brain syndrome. [EU]

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]

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

Deoxyguanosine: A nucleoside consisting of the base guanine and the sugar deoxyribose. [NIH]

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

Dermis: A layer of vascular connective tissue underneath the epidermis. The surface of the dermis contains sensitive papillae. Embedded in or beneath the dermis are sweat glands, hair follicles, and sebaceous glands. [NIH]

Deuterium: Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [NIH]

Developed Countries: Countries that have reached a level of economic achievement through an increase of production, per capita income and consumption, and utilization of natural and human resources. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

Diabetic Foot: Ulcers of the foot as a complication of diabetes. Diabetic foot, often with infection, is a common serious complication of diabetes and may require hospitalization and disfiguring surgery. The foot ulcers are probably secondary to neuropathies and vascular problems. [NIH]

Diabetic Ketoacidosis: Complication of diabetes resulting from severe insulin deficiency coupled with an absolute or relative increase in glucagon concentration. The metabolic acidosis is caused by the breakdown of adipose stores and resulting increased levels of free fatty acids. Glucagon accelerates the oxidation of the free fatty acids producing excess ketone bodies (ketosis). [NIH]

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

Dialyzer: A part of the hemodialysis machine. (See hemodialysis under dialysis.) The dialyzer has two sections separated by a membrane. One section holds dialysate. The other holds the patient's blood. [NIH]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diastole: Period of relaxation of the heart, especially the ventricles. [NIH]

Diastolic: Of or pertaining to the diastole. [EU]

Diastolic blood pressure: The minimum pressure that remains within the artery when the heart is at rest. [NIH]

Dietary Fats: Fats present in food, especially in animal products such as meat, meat products, butter, ghee. They are present in lower amounts in nuts, seeds, and avocados. [NIH]

Dietary Fiber: The remnants of plant cell walls that are resistant to digestion by the alimentary enzymes of man. It comprises various polysaccharides and lignins. [NIH]

Dietitian: An expert in nutrition who helps people plan what and how much food to eat. [NIH]

Diffusion: The tendency of a gas or solute to pass from a point of higher pressure or concentration to a point of lower pressure or concentration and to distribute itself throughout the available space; a major mechanism of biological transport. [NIH]

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

Digestive tract: The organs through which food passes when food is eaten. These organs are the mouth, esophagus, stomach, small and large intestines, and rectum. [NIH]

Dihydrotestosterone: Anabolic agent. [NIH]

Dihydroxy: AMPA/Kainate antagonist. [NIH]

Dilatation, Pathologic: The condition of an anatomical structure's being dilated beyond normal dimensions. [NIH]

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

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

Discrete: Made up of separate parts or characterized by lesions which do not become blended; not running together; separate. [NIH]

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

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]

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

Dopamine: An endogenous catecholamine and prominent neurotransmitter in several systems of the brain. In the synthesis of catecholamines from tyrosine, it is the immediate precursor to norepinephrine and epinephrine. Dopamine is a major transmitter in the extrapyramidal system of the brain, and important in regulating movement. A family of dopaminergic receptor subtypes mediate its action. Dopamine is used pharmacologically for its direct (beta adrenergic agonist) and indirect (adrenergic releasing) sympathomimetic effects including its actions as an inotropic agent and as a renal vasodilator. [NIH]

Double-blind: Pertaining to a clinical trial or other experiment in which neither the subject nor the person administering treatment knows which treatment any particular subject is receiving. [EU]

Drug Interactions: The action of a drug that may affect the activity, metabolism, or toxicity

of another drug. [NIH]

Drug Resistance: Diminished or failed response of an organism, disease or tissue to the intended effectiveness of a chemical or drug. It should be differentiated from drug tolerance which is the progressive diminution of the susceptibility of a human or animal to the effects of a drug, as a result of continued administration. [NIH]

Drug Tolerance: Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

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

Duodenum: The first part of the small intestine. [NIH]

Dyes: Chemical substances that are used to stain and color other materials. The coloring may or may not be permanent. Dyes can also be used as therapeutic agents and test reagents in medicine and scientific research. [NIH]

Dyskinesia: Impairment of the power of voluntary movement, resulting in fragmentary or incomplete movements. [EU]

Dyslipidemia: Disorders in the lipoprotein metabolism; classified as hypercholesterolemia, hypertriglyceridemia, combined hyperlipidemia, and low levels of high-density lipoprotein (HDL) cholesterol. All of the dyslipidemias can be primary or secondary. Both elevated levels of low-density lipoprotein (LDL) cholesterol and low levels of HDL cholesterol predispose to premature atherosclerosis. [NIH]

Dyspnea: Difficult or labored breathing. [NIH]

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

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

Ego: The conscious portion of the personality structure which serves to mediate between the demands of the primitive instinctual drives, (the id), of internalized parental and social prohibitions or the conscience, (the superego), and of reality. [NIH]

Elastic: Susceptible of resisting and recovering from stretching, compression or distortion applied by a force. [EU]

Elasticity: Resistance and recovery from distortion of shape. [NIH]

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

Electrolysis: Destruction by passage of a galvanic electric current, as in disintegration of a chemical compound in solution. [NIH]

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

Electrons: Stable elementary particles having the smallest known negative charge, present in

all elements; also called negatrons. Positively charged electrons are called positrons. The numbers, energies and arrangement of electrons around atomic nuclei determine the chemical identities of elements. Beams of electrons are called cathode rays or beta rays, the latter being a high-energy biproduct of nuclear decay. [NIH]

Electrophoresis: An electrochemical process in which macromolecules or colloidal particles with a net electric charge migrate in a solution under the influence of an electric current. [NIH]

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]

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]

Endemic: Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

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

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]

Endocrinology: A subspecialty of internal medicine concerned with the metabolism, physiology, and disorders of the endocrine system. [NIH]

Endogenous: Produced inside an organism or cell. The opposite is external (exogenous) production. [NIH]

Endometrial: Having to do with the endometrium (the layer of tissue that lines the uterus). [NIH]

Endometrium: The layer of tissue that lines the uterus. [NIH]

Endopeptidases: A subclass of peptide hydrolases. They are classified primarily by their catalytic mechanism. Specificity is used only for identification of individual enzymes. They comprise the serine endopeptidases, EC 3.4.21; cysteine endopeptidases, EC 3.4.22; aspartic endopeptidases, EC 3.4.23, metalloendopeptidases, EC 3.4.24; and a group of enzymes yet to be assigned to any of the above sub-classes, EC 3.4.99. EC 3.4.-. [NIH]

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]

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]

Endotoxins: Toxins closely associated with the living cytoplasm or cell wall of certain microorganisms, which do not readily diffuse into the culture medium, but are released upon lysis of the cells. [NIH]

End-stage renal: Total chronic kidney failure. When the kidneys fail, the body retains fluid and harmful wastes build up. A person with ESRD needs treatment to replace the work of the failed kidneys. [NIH]

Energy balance: Energy is the capacity of a body or a physical system for doing work. Energy balance is the state in which the total energy intake equals total energy needs. [NIH]

Energy Intake: Total number of calories taken in daily whether ingested or by parenteral routes. [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]

Enteritis: Inflammation of the intestine, applied chiefly to inflammation of the small intestine; see also enterocolitis. [EU]

Enterocolitis: Inflammation of the intestinal mucosa of the small and large bowel. [NIH]

Environmental Health: The science of controlling or modifying those conditions, influences, or forces surrounding man which relate to promoting, establishing, and maintaining health. [NIH]

Enzymatic: Phase where enzyme cuts the precursor protein. [NIH]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

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

Epidemiological: Relating to, or involving epidemiology. [EU]

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]

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

Erectile: The inability to get or maintain an erection for satisfactory sexual intercourse. Also

called impotence. [NIH]

Erection: The condition of being made rigid and elevated; as erectile tissue when filled with blood. [EU]

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

Erythropoietin: Glycoprotein hormone, secreted chiefly by the kidney in the adult and the liver in the fetus, that acts on erythroid stem cells of the bone marrow to stimulate proliferation and differentiation. [NIH]

Escalation: Progressive use of more harmful drugs. [NIH]

Esophageal: Having to do with the esophagus, the muscular tube through which food passes from the throat to the stomach. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Estradiol: The most potent mammalian estrogenic hormone. It is produced in the ovary, placenta, testis, and possibly the adrenal cortex. [NIH]

Estrogen: One of the two female sex hormones. [NIH]

Estrogen receptor: ER. Protein found on some cancer cells to which estrogen will attach. [NIH]

Estrogen Receptor Modulators: Substances that possess antiestrogenic actions but can also produce estrogenic effects as well. They act as complete or partial agonist or as antagonist. They can be either steroidal or nonsteroidal in structure. [NIH]

Estrone: 3-Hydroxyestra-1,3,5(10)-trien-17-one. A metabolite of estradiol but possessing less biological activity. It is found in the urine of pregnant women and mares, in the human placenta, and in the urine of bulls and stallions. According to the Fourth Annual Report on Carcinogens (NTP 85-002, 1985), estrone may reasonably be anticipated to be a carcinogen (Merck, 11th ed). [NIH]

Ethanol: A clear, colorless liquid rapidly absorbed from the gastrointestinal tract and distributed throughout the body. It has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations as well as serving as the primary ingredient in alcoholic beverages. [NIH]

Ether: One of a class of organic compounds in which any two organic radicals are attached directly to a single oxygen atom. [NIH]

Ethylnitrosourea: A nitrosourea compound with alkylating, carcinogenic, and mutagenic properties. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Evacuation: An emptying, as of the bowels. [EU]

Evoke: The electric response recorded from the cerebral cortex after stimulation of a peripheral sense organ. [NIH]

Excipients: Usually inert substances added to a prescription in order to provide suitable consistency to the dosage form; a binder, matrix, base or diluent in pills, tablets, creams, salves, etc. [NIH]

Excisional: The surgical procedure of removing a tumor by cutting it out. The biopsy is then examined under a microscope. [NIH]

Excitation: An act of irritation or stimulation or of responding to a stimulus; the addition of energy, as the excitation of a molecule by absorption of photons. [EU]

Excrete: To get rid of waste from the body. [NIH]

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]

Exhaustion: The feeling of weariness of mind and body. [NIH]

Exocrine: Secreting outwardly, via a duct. [EU]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Expiration: The act of breathing out, or expelling air from the lungs. [EU]

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]

Extrapyramidal: Outside of the pyramidal tracts. [EU]

Extravasation: A discharge or escape, as of blood, from a vessel into the tissues. [EU]

Extremity: A limb; an arm or leg (membrum); sometimes applied specifically to a hand or foot. [EU]

Eye Infections: Infection, moderate to severe, caused by bacteria, fungi, or viruses, which occurs either on the external surface of the eye or intraocularly with probable inflammation, visual impairment, or blindness. [NIH]

Failure to Thrive: A condition in which an infant or child's weight gain and growth are far below usual levels for age. [NIH]

Familial polyposis: An inherited condition in which numerous polyps (tissue masses) develop on the inside walls of the colon and rectum. It increases the risk for colon cancer. [NIH]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Fat: Total lipids including phospholipids. [NIH]

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 Liver: The buildup of fat in liver cells. The most common cause is alcoholism. Other causes include obesity, diabetes, and pregnancy. Also called steatosis. [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 Death: Death of the young developing in utero. [NIH]

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

Fetoprotein: Transabdominal aspiration of fluid from the amniotic sac with a view to detecting increases of alpha-fetoprotein in maternal blood during pregnancy, as this is an important indicator of open neural tube defects in the fetus. [NIH]

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

Fibrinolytic: Pertaining to, characterized by, or causing the dissolution of fibrin by enzymatic action [EU]

Fibroblast Growth Factor: Peptide isolated from the pituitary gland and from the brain. It is a potent mitogen which stimulates growth of a variety of mesodermal cells including chondrocytes, granulosa, and endothelial cells. The peptide may be active in wound healing and animal limb regeneration. [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]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

Fissure: Any cleft or groove, normal or otherwise; especially a deep fold in the cerebral cortex which involves the entire thickness of the brain wall. [EU]

Flank Pain: Pain emanating from below the ribs and above the ilium. [NIH]

Flatus: Gas passed through the rectum. [NIH]

Flavoring Agents: Substances added to foods and medicine to improve the quality of taste. [NIH]

Flow Cytometry: Technique using an instrument system for making, processing, and displaying one or more measurements on individual cells obtained from a cell suspension.

Cells are usually stained with one or more fluorescent dyes specific to cell components of interest, e.g., DNA, and fluorescence of each cell is measured as it rapidly transverses the excitation beam (laser or mercury arc lamp). Fluorescence provides a quantitative measure of various biochemical and biophysical properties of the cell, as well as a basis for cell sorting. Other measurable optical parameters include light absorption and light scattering, the latter being applicable to the measurement of cell size, shape, density, granularity, and stain uptake. [NIH]

Fluid Therapy: Therapy whose basic objective is to restore the volume and composition of the body fluids to normal with respect to water-electrolyte balance. Fluids may be administered intravenously, orally, by intermittent gavage, or by hypodermoclysis. [NIH]

Fluorescence: The property of emitting radiation while being irradiated. The radiation emitted is usually of longer wavelength than that incident or absorbed, e.g., a substance can be irradiated with invisible radiation and emit visible light. X-ray fluorescence is used in diagnosis. [NIH]

Fluorescent Dyes: Dyes that emit light when exposed to light. The wave length of the emitted light is usually longer than that of the incident light. Fluorochromes are substances that cause fluorescence in other substances, i.e., dyes used to mark or label other compounds with fluorescent tags. They are used as markers in biochemistry and immunology. [NIH]

Flush: Transient, episodic redness of the face and neck caused by certain diseases, ingestion of certain drugs or other substances, heat, emotional factors, or physical exertion. [EU]

Flushing: A transient reddening of the face that may be due to fever, certain drugs, exertion, stress, or a disease process. [NIH]

Foam Cells: Lipid-laden macrophages originating from monocytes or from smooth muscle cells. [NIH]

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

Fold: A plication or doubling of various parts of the body. [NIH]

Folic Acid: N-(4-(((2-Amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl)amino)benzoyl)-L-glutamic acid. A member of the vitamin B family that stimulates the hematopoietic system. It is present in the liver and kidney and is found in mushrooms, spinach, yeast, green leaves, and grasses. Folic acid is used in the treatment and prevention of folate deficiencies and megaloblastic anemia. [NIH]

Food Additives: Substances which are of little or no nutritive value, but are used in the processing or storage of foods or animal feed, especially in the developed countries; includes antioxidants, food preservatives, food coloring agents, flavoring agents, anti-infective agents (both plain and local), vehicles, excipients and other similarly used substances. Many of the same substances are pharmaceutic aids when added to pharmaceuticals rather than to foods. [NIH]

Food Coloring Agents: Natural or synthetic dyes used as coloring agents in processed foods. [NIH]

Food Hypersensitivity: Gastrointestinal disturbances, skin eruptions, or shock due to allergic reactions to allergens ingested in food. [NIH]

Food Labeling: Use of written, printed, or graphic materials upon or accompanying a food or its container or wrapper. The concept includes ingredients, nutritional value, directions, warnings, and other relevant information. [NIH]

Food Preservatives: Substances capable of inhibiting, retarding or arresting the process of fermentation, acidification or other deterioration of foods. [NIH]

Foot Ulcer: Lesion on the surface of the skin of the foot, usually accompanied by inflammation. The lesion may become infected or necrotic and is frequently associated with diabetes or leprosy. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Free Radicals: Highly reactive molecules with an unsatisfied electron valence pair. Free radicals are produced in both normal and pathological processes. They are proven or suspected agents of tissue damage in a wide variety of circumstances including radiation, damage from environment chemicals, and aging. Natural and pharmacological prevention of free radical damage is being actively investigated. [NIH]

Fulminant Hepatic Failure: Liver failure that occurs suddenly in a previously healthy person. The most common causes of FHF are acute hepatitis, acetaminophen overdose, and liver damage from prescription drugs. [NIH]

Fungus: A general term used to denote a group of eukaryotic protists, including mushrooms, yeasts, rusts, moulds, smuts, etc., which are characterized by the absence of chlorophyll and by the presence of a rigid cell wall composed of chitin, mannans, and sometimes cellulose. They are usually of simple morphological form or show some reversible cellular specialization, such as the formation of pseudoparenchymatous tissue in the fruiting body of a mushroom. The dimorphic fungi grow, according to environmental conditions, as moulds or yeasts. [EU]

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]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastric Bypass: Surgical procedure in which the stomach is transected high on the body. The resulting proximal remnant is joined to a loop of the jejunum in an end-to-side anastomosis. This procedure is used frequently in the treatment of morbid obesity. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gastritis: Inflammation of the stomach. [EU]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [NIH]

Gastrostomy: Creation of an artificial external opening into the stomach for nutritional support or gastrointestinal compression. [NIH]

Gavage: Feeding by a tube passed into the stomach; called also tube feeding. [NIH]

Gelatin: A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [NIH]

Gemfibrozil: A lipid-regulating agent that lowers elevated serum lipids primarily by decreasing serum triglycerides with a variable reduction in total cholesterol. These decreases occur primarily in the VLDL fraction and less frequently in the LDL fraction. Gemfibrozil increases HDL subfractions HDL2 and HDL3 as well as apolipoproteins A-I and A-II. Its mechanism of action has not been definitely established. [NIH]

Gene: The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein.

[NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Gene Expression Profiling: The determination of the pattern of genes expressed i.e., transcribed, under specific circumstances or in a specific cell. [NIH]

Gene Therapy: The introduction of new genes into cells for the purpose of treating disease by restoring or adding gene expression. Techniques include insertion of retroviral vectors, transfection, homologous recombination, and injection of new genes into the nuclei of single cell embryos. The entire gene therapy process may consist of multiple steps. The new genes may be introduced into proliferating cells in vivo (e.g., bone marrow) or in vitro (e.g., fibroblast cultures) and the modified cells transferred to the site where the gene expression is required. Gene therapy may be particularly useful for treating enzyme deficiency diseases, hemoglobinopathies, and leukemias and may also prove useful in restoring drug sensitivity, particularly for leukemia. [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 Techniques: Chromosomal, biochemical, intracellular, and other methods used in the study of genetics. [NIH]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genital: Pertaining to the genitalia. [EU]

Genomics: The systematic study of the complete DNA sequences (genome) of organisms. [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]

Gland: An organ that produces and releases one or more substances for use in the body. Some glands produce fluids that affect tissues or organs. Others produce hormones or participate in blood production. [NIH]

Glomerular: Pertaining to or of the nature of a glomerulus, especially a renal glomerulus. [EU]

Glomerular Filtration Rate: The volume of water filtered out of plasma through glomerular capillary walls into Bowman's capsules per unit of time. It is considered to be equivalent to inulin clearance. [NIH]

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]

Glomerulus: A tiny set of looping blood vessels in the nephron where blood is filtered in the kidney. [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]

Gluconeogenesis: The process by which glucose is formed from a non-carbohydrate source. [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]

Glucose tolerance: The power of the normal liver to absorb and store large quantities of glucose and the effectiveness of intestinal absorption of glucose. The glucose tolerance test is a metabolic test of carbohydrate tolerance that measures active insulin, a hepatic function based on the ability of the liver to absorb glucose. The test consists of ingesting 100 grams of glucose into a fasting stomach; blood sugar should return to normal in 2 to 21 hours after ingestion. [NIH]

Glucose Tolerance Test: Determination of whole blood or plasma sugar in a fasting state before and at prescribed intervals (usually 1/2 hr, 1 hr, 3 hr, 4 hr) after taking a specified amount (usually 100 gm orally) of glucose. [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]

Glutamic Acid: A non-essential amino acid naturally occurring in the L-form. Glutamic acid (glutamate) is the most common excitatory neurotransmitter in the central nervous system. [NIH]

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]

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]

Glycolysis: The pathway by which glucose is catabolized into two molecules of pyruvic acid with the generation of ATP. [NIH]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Glycosaminoglycan: A type of long, unbranched polysaccharide molecule. Glycosaminoglycans are major structural components of cartilage and are also found in the cornea of the eye. [NIH]

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]

Gonadal: Pertaining to a gonad. [EU]

Gonads: The gamete-producing glands, ovary or testis. [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]

Grafting: The operation of transfer of tissue from one site to another. [NIH]

Gram-negative: Losing the stain or decolorized by alcohol in Gram's method of staining, a primary characteristic of bacteria having a cell wall composed of a thin layer of peptidoglycan covered by an outer membrane of lipoprotein and lipopolysaccharide. [EU]

Gram-positive: Retaining the stain or resisting decolorization by alcohol in Gram's method of staining, a primary characteristic of bacteria whose cell wall is composed of a thick layer of peptidologlycan with attached teichoic acids. [EU]

Gram-Positive Bacteria: Bacteria which retain the crystal violet stain when treated by Gram's method. [NIH]

Grasses: A large family, Gramineae, of narrow-leaved herbaceous monocots. Many grasses produce highly allergenic pollens and are hosts to cattle parasites and toxic fungi. [NIH]

Growth 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]

Guanine: One of the four DNA bases. [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]

Haptens: Small antigenic determinants capable of eliciting an immune response only when coupled to a carrier. Haptens bind to antibodies but by themselves cannot elicit an antibody response. [NIH]

Headache: Pain in the cranial region that may occur as an isolated and benign symptom or as a manifestation of a wide variety of conditions including subarachnoid hemorrhage; craniocerebral trauma; central nervous system infections; intracranial hypertension; and other disorders. In general, recurrent headaches that are not associated with a primary disease process are referred to as headache disorders (e.g., migraine). [NIH]

Headache Disorders: Common conditions characterized by persistent or recurrent headaches. Headache syndrome classification systems may be based on etiology (e.g., vascular headache, post-traumatic headaches, etc.), temporal pattern (e.g., cluster headache, paroxysmal hemicrania, etc.), and precipitating factors (e.g., cough headache). [NIH]

Health Promotion: Encouraging consumer behaviors most likely to optimize health potentials (physical and psychosocial) through health information, preventive programs, and access to medical care. [NIH]

Health Services: Services for the diagnosis and treatment of disease and the maintenance of health. [NIH]

Health Status: The level of health of the individual, group, or population as subjectively assessed by the individual or by more objective measures. [NIH]

Heart attack: A seizure of weak or abnormal functioning of the heart. [NIH]

Heart failure: Loss of pumping ability by the heart, often accompanied by fatigue, breathlessness, and excess fluid accumulation in body tissues. [NIH]

Heart Transplantation: The transference of a heart from one human or animal to another. [NIH]

Heart Valves: Flaps of tissue that prevent regurgitation of blood from the ventricles to the atria or from the pulmonary arteries or aorta to the ventricles. [NIH]

Helicobacter: A genus of gram-negative, spiral-shaped bacteria that is pathogenic and has been isolated from the intestinal tract of mammals, including humans. [NIH]

Helicobacter pylori: A spiral bacterium active as a human gastric pathogen. It is a gram-negative, urease-positive, curved or slightly spiral organism initially isolated in 1982 from patients with lesions of gastritis or peptic ulcers in Western Australia. Helicobacter pylori was originally classified in the genus Campylobacter, but RNA sequencing, cellular fatty acid profiles, growth patterns, and other taxonomic characteristics indicate that the micro-organism should be included in the genus Helicobacter. It has been officially transferred to Helicobacter gen. nov. (see Int J Syst Bacteriol 1989 Oct;39(4):297-405). [NIH]

Hematocrit: Measurement of the volume of packed red cells in a blood specimen by centrifugation. The procedure is performed using a tube with graduated markings or with automated blood cell counters. It is used as an indicator of erythrocyte status in disease. For example, anemia shows a low hematocrit, polycythemia, high values. [NIH]

Hematoma: An extravasation of blood localized in an organ, space, or tissue. [NIH]

Hematuria: Presence of blood in the urine. [NIH]

Heme: The color-furnishing portion of hemoglobin. It is found free in tissues and as the prosthetic group in many hemeproteins. [NIH]

Hemodialysis: The use of a machine to clean wastes from the blood after the kidneys have failed. The blood travels through tubes to a dialyzer, which removes wastes and extra fluid. The cleaned blood then flows through another set of tubes back into the body. [NIH]

Hemoglobin: One of the fractions of glycosylated hemoglobin A1c. Glycosylated hemoglobin is formed when linkages of glucose and related monosaccharides bind to hemoglobin A and its concentration represents the average blood glucose level over the previous several weeks. HbA1c levels are used as a measure of long-term control of plasma glucose (normal, 4 to 6 percent). In controlled diabetes mellitus, the concentration of glycosylated hemoglobin A is within the normal range, but in uncontrolled cases the level may be 3 to 4 times the normal conentration. Generally, complications are substantially lower among patients with Hb levels of 7 percent or less than in patients with HbA1c levels of 9 percent or more. [NIH]

Hemoglobinopathies: A group of inherited disorders characterized by structural alterations within the hemoglobin molecule. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [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]

Hepatotoxicity: How much damage a medicine or other substance does to the liver. [NIH]

Hereditary: Of, relating to, or denoting factors that can be transmitted genetically from one generation to another. [NIH]

Heredity: 1. The genetic transmission of a particular quality or trait from parent to offspring. 2. The genetic constitution of an individual. [EU]

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]

High-density lipoproteins: Lipoproteins that contain a small amount of cholesterol and carry cholesterol away from body cells and tissues to the liver for excretion from the body. Low-level HDL increases the risk of heart disease, so the higher the HDL level, the better. The HDL component normally contains 20 to 30 percent of total cholesterol, and HDL levels are inversely correlated with coronary heart disease risk. [NIH]

Histamine: 1H-Imidazole-4-ethanamine. A depressor amine derived by enzymatic decarboxylation of histidine. It is a powerful stimulant of gastric secretion, a constrictor of bronchial smooth muscle, a vasodilator, and also a centrally acting neurotransmitter. [NIH]

Histones: Small chromosomal proteins (approx 12-20 kD) possessing an open, unfolded structure and attached to the DNA in cell nuclei by ionic linkages. Classification into the various types (designated histone I, histone II, etc.) is based on the relative amounts of arginine and lysine in each. [NIH]

Homeostasis: The processes whereby the internal environment of an organism tends to remain balanced and stable. [NIH]

Homologous: Corresponding in structure, position, origin, etc., as (a) the feathers of a bird and the scales of a fish, (b) antigen and its specific antibody, (c) allelic chromosomes. [EU]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Housekeeping: The care and management of property. [NIH]

Human growth hormone: A protein hormone, secreted by the anterior lobe of the pituitary, which promotes growth of the whole body by stimulating protein synthesis. The human gene has already been cloned and successfully expressed in bacteria. [NIH]

Humoral: Of, relating to, proceeding from, or involving a bodily humour - now often used of endocrine factors as opposed to neural or somatic. [EU]

Humour: 1. A normal functioning fluid or semifluid of the body (as the blood, lymph or bile) especially of vertebrates. 2. A secretion that is itself an excitant of activity (as certain hormones). [EU]

Hybrid: Cross fertilization between two varieties or, more usually, two species of vines, see also crossing. [NIH]

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]

Hydroxy Acids: Organic compounds containing both the hydroxyl and carboxyl radicals. [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]

Hypercholesterolemia: Abnormally high levels of cholesterol in the blood. [NIH]

Hypercholesterolemia, Familial: A familial disorder characterized by increased plasma concentration of cholesterol carried in low density lipoproteins (LDL) and by a deficiency in a cell surface receptor which regulates LDL degradation and cholesterol synthesis. [NIH]

Hyperglycemia: Abnormally high blood sugar. [NIH]

Hyperhomocysteinemia: An inborn error of methionone metabolism which produces an excess of homocysteine in the blood. It is often caused by a deficiency of cystathionine beta-synthase and is a risk factor for coronary vascular disease. [NIH]

Hyperlipoproteinemia: Metabolic disease characterized by elevated plasma cholesterol and/or triglyceride levels. The inherited form is attributed to a single gene mechanism. [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]

Hypersensitivity: Altered reactivity to an antigen, which can result in pathologic reactions upon subsequent exposure to that particular antigen. [NIH]

Hypertension: Persistently high arterial blood pressure. Currently accepted threshold levels are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [NIH]

Hyperthyroidism: Excessive functional activity of the thyroid gland. [NIH]

Hypertriglyceridemia: Condition of elevated triglyceride concentration in the blood; an inherited form occurs in familial hyperlipoproteinemia IIb and hyperlipoproteinemia type IV. It has been linked to higher risk of heart disease and arteriosclerosis. [NIH]

Hypertrophy: General increase in bulk of a part or organ, not due to tumor formation, nor to an increase in the number of cells. [NIH]

Hyperuricemia: A buildup of uric acid (a byproduct of metabolism) in the blood; a side effect of some anticancer drugs. [NIH]

Hypnotic: A drug that acts to induce sleep. [EU]

Hypoglycemia: Abnormally low blood sugar [NIH]

Hypoglycemic: An orally active drug that produces a fall in blood glucose concentration. [NIH]

Hypoglycemic Agents: Agents which lower the blood glucose level. [NIH]

Hypolipidemic: A drug that lowers abnormally high plasma concentrations of cholesterol or triglycerides or both. [NIH]

Hypotension: Abnormally low blood pressure. [NIH]

Hypothalamic: Of or involving the hypothalamus. [EU]

Hypothalamus: Ventral part of the diencephalon extending from the region of the optic chiasm to the caudal border of the mammillary bodies and forming the inferior and lateral walls of the third ventricle. [NIH]

Hypoxanthine: A purine and a reaction intermediate in the metabolism of adenosine and in the formation of nucleic acids by the salvage pathway. [NIH]

Hypoxia: Reduction of oxygen supply to tissue below physiological levels despite adequate perfusion of the tissue by blood. [EU]

Hypoxic: Having too little oxygen. [NIH]

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]

Ileal: Related to the ileum, the lowest end of the small intestine. [NIH]

Ileum: The lower end of the small intestine. [NIH]

Illusion: A false interpretation of a genuine percept. [NIH]

Immune function: Production and action of cells that fight disease or infection. [NIH]

Immune response: The activity of the immune system against foreign substances (antigens). [NIH]

Immune system: The organs, cells, and molecules responsible for the recognition and disposal of foreign ("non-self") material which enters the body. [NIH]

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]

Immunochemistry: Field of chemistry that pertains to immunological phenomena and the study of chemical reactions related to antigen stimulation of tissues. It includes physicochemical interactions between antigens and antibodies. [NIH]

Immunodeficiency: The decreased ability of the body to fight infection and disease. [NIH]

Immunogenic: Producing immunity; evoking an immune response. [EU]

Immunoglobulin: A protein that acts as an antibody. [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]

Immunophilin: A drug for the treatment of Parkinson's disease. [NIH]

Immunosuppressive: Describes the ability to lower immune system responses. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

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]

Impotence: The inability to perform sexual intercourse. [NIH]

Impotency: Lack of power in the male to copulate, i. e. inability to achieve penile erection; the cause may be exposure to organic solvents or other toxic substances. [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]

Incontinence: Inability to control the flow of urine from the bladder (urinary incontinence) or the escape of stool from the rectum (fecal incontinence). [NIH]

Indinavir: A potent and specific HIV protease inhibitor that appears to have good oral bioavailability. [NIH]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Infancy: The period of complete dependency prior to the acquisition of competence in walking, talking, and self-feeding. [NIH]

Infant Nutrition: Nutrition of children from birth to 2 years of age. [NIH]

Infant, Newborn: An infant during the first month after birth. [NIH]

Infantile: Pertaining to an infant or to infancy. [EU]

Infarction: A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

Infection: 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local infection may persist and spread by extension to become an acute, subacute, or chronic

clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

Infiltration: The diffusion or accumulation in a tissue or cells of substances not normal to it or in amounts of the normal. Also, the material so accumulated. [EU]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Inflammatory bowel disease: A general term that refers to the inflammation of the colon and rectum. Inflammatory bowel disease includes ulcerative colitis and Crohn's disease. [NIH]

Infusion: A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

Ingestion: Taking into the body by mouth [NIH]

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]

Inotropic: Affecting the force or energy of muscular contractions. [EU]

Insight: The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Insomnia: Difficulty in going to sleep or getting enough sleep. [NIH]

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]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

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]

Intramuscular: IM. Within or into muscle. [NIH]

Intravascular: Within a vessel or vessels. [EU]

Intravenous: IV. Into a vein. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

Inulin: A starch found in the tubers and roots of many plants. Since it is hydrolyzable to fructose, it is classified as a fructosan. It has been used in physiologic investigation for

determination of the rate of glomerular function. [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]

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]

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]

Irritable Bowel Syndrome: A disorder that comes and goes. Nerves that control the muscles in the GI tract are too active. The GI tract becomes sensitive to food, stool, gas, and stress. Causes abdominal pain, bloating, and constipation or diarrhea. Also called spastic colon or mucous colitis. [NIH]

Ischemia: Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel. [EU]

Isoflavones: 3-Phenylchromones. Isomeric form of flavones in which the benzene group is attached to the 3 position of the benzopyran ring instead of the 2 position. [NIH]

Jejunostomy: Surgical formation of an opening through the abdominal wall into the jejunum, usually for enteral hyperalimentation. [NIH]

Jejunum: That portion of the small intestine which extends from the duodenum to the ileum; called also intestinum jejunum. [EU]

Jugular Veins: Veins in the neck which drain the brain, face, and neck into the brachiocephalic or subclavian veins. [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]

Keratoconjunctivitis: Simultaneous inflammation of the cornea and conjunctiva. [NIH]

Keratoconjunctivitis Sicca: Drying and inflammation of the conjunctiva as a result of insufficient lacrimal secretion. When found in association with xerostomia and polyarthritis, it is called Sjogren's syndrome. [NIH]

Ketoacidosis: Acidosis accompanied by the accumulation of ketone bodies (ketosis) in the body tissues and fluids, as in diabetic acidosis. [EU]

Ketone Bodies: Chemicals that the body makes when there is not enough insulin in the blood and it must break down fat for its energy. Ketone bodies can poison and even kill body cells. When the body does not have the help of insulin, the ketones build up in the

blood and then "spill" over into the urine so that the body can get rid of them. The body can also rid itself of one type of ketone, called acetone, through the lungs. This gives the breath a fruity odor. Ketones that build up in the body for a long time lead to serious illness and coma. [NIH]

Ketosis: A condition of having ketone bodies build up in body tissues and fluids. The signs of ketosis are nausea, vomiting, and stomach pain. Ketosis can lead to ketoacidosis. [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 Transplantation: The transference of a kidney from one human or animal to another. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Kringles: Triple-looped protein domains linked by disulfide bonds. These common structural domains, so-named for their resemblance to Danish pastries known as kringlers, play a role in binding membranes, proteins, and phospholipids as well as in regulating proteolysis. Kringles are also present in coagulation-related and fibrinolytic proteins and other plasma proteinases. [NIH]

Labile: 1. Gliding; moving from point to point over the surface; unstable; fluctuating. 2. Chemically unstable. [EU]

Labyrinth: The internal ear; the essential part of the organ of hearing. It consists of an osseous and a membranous portion. [NIH]

Labyrinthine: A vestibular nystagmus resulting from stimulation, injury, or disease of the labyrinth. [NIH]

Lacrimal: Pertaining to the tears. [EU]

Lactobacillus: A genus of gram-positive, microaerophilic, rod-shaped bacteria occurring widely in nature. Its species are also part of the many normal flora of the mouth, intestinal tract, and vagina of many mammals, including humans. Pathogenicity from this genus is rare. [NIH]

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]

Latent: Phoria which occurs at one distance or another and which usually has no troublesome effect. [NIH]

Laxative: An agent that acts to promote evacuation of the bowel; a cathartic or purgative. [EU]

Leptin: A 16-kD peptide hormone secreted from white adipocytes and implicated in the regulation of food intake and energy balance. Leptin provides the key afferent signal from fat cells in the feedback system that controls body fat stores. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Leucine: An essential branched-chain amino acid important for hemoglobin formation. [NIH]

Leukapheresis: The preparation of leukocyte concentrates with the return of red cells and leukocyte-poor plasma to the donor. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Leukocytes: White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

Libido: The psychic drive or energy associated with sexual instinct in the broad sense (pleasure and love-object seeking). It may also connote the psychic energy associated with instincts in general that motivate behavior. [NIH]

Life cycle: The successive stages through which an organism passes from fertilized ovum or spore to the fertilized ovum or spore of the next generation. [NIH]

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]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Lipase: An enzyme of the hydrolase class that catalyzes the reaction of triacylglycerol and water to yield diacylglycerol and a fatty acid anion. It is produced by glands on the tongue and by the pancreas and initiates the digestion of dietary fats. (From Dorland, 27th ed) EC 3.1.1.3. [NIH]

Lipid: Fat. [NIH]

Lipid A: Lipid A is the biologically active component of lipopolysaccharides. It shows strong endotoxic activity and exhibits immunogenic properties. [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]

Lipolysis: The hydrolysis of lipids. [NIH]

Lipopolysaccharides: Substance consisting of polysaccaride and lipid. [NIH]

Lipoprotein: Any of the lipid-protein complexes in which lipids are transported in the blood; lipoprotein particles consist of a spherical hydrophobic core of triglycerides or cholesterol esters surrounded by an amphipathic monolayer of phospholipids, cholesterol, and apolipoproteins; the four principal classes are high-density, low-density, and very-low-density lipoproteins and chylomicrons. [EU]

Lipoprotein Lipase: An enzyme of the hydrolase class that catalyzes the reaction of

triacylglycerol and water to yield diacylglycerol and a fatty acid anion. The enzyme hydrolyzes triacylglycerols in chylomicrons, very-low-density lipoproteins, low-density lipoproteins, and diacylglycerols. It occurs on capillary endothelial surfaces, especially in mammary, muscle, and adipose tissue. Genetic deficiency of the enzyme causes familial hyperlipoproteinemia Type I. (Dorland, 27th ed) EC 3.1.1.34. [NIH]

Lithium: An element in the alkali metals family. It has the atomic symbol Li, atomic number 3, and atomic weight 6.94. Salts of lithium are used in treating manic-depressive disorders. [NIH]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

Liver Cirrhosis: Liver disease in which the normal microcirculation, the gross vascular anatomy, and the hepatic architecture have been variably destroyed and altered with fibrous septa surrounding regenerated or regenerating parenchymal nodules. [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]

Localization: The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

Localized: Cancer which has not metastasized yet. [NIH]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

Long-Term Care: Care over an extended period, usually for a chronic condition or disability, requiring periodic, intermittent, or continuous care. [NIH]

Loop: A wire usually of platinum bent at one end into a small loop (usually 4 mm inside diameter) and used in transferring microorganisms. [NIH]

Lovastatin: A fungal metabolite isolated from cultures of Aspergillus terreus. The compound is a potent anticholesteremic agent. It inhibits 3-hydroxy-3-methylglutaryl coenzyme A reductase (hydroxymethylglutaryl CoA reductases), which is the rate-limiting enzyme in cholesterol biosynthesis. It also stimulates the production of low-density lipoprotein receptors in the liver. [NIH]

Low-density lipoprotein: Lipoprotein that contains most of the cholesterol in the blood. LDL carries cholesterol to the tissues of the body, including the arteries. A high level of LDL increases the risk of heart disease. LDL typically contains 60 to 70 percent of the total serum cholesterol and both are directly correlated with CHD risk. [NIH]

Lubricants: Oily or slippery substances. [NIH]

Luciferase: Any one of several enzymes that catalyze the bioluminescent reaction in certain marine crustaceans, fish, bacteria, and insects. The enzyme is a flavoprotein; it oxidizes luciferins to an electronically excited compound that emits energy in the form of light. The

color of light emitted varies with the organism. The firefly enzyme is a valuable reagent for measurement of ATP concentration. (Dorland, 27th ed) EC 1.13.12.-. [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 Metastasis: Transfer of a neoplasm from its primary site to lymph nodes or to distant parts of the body by way of the lymphatic system. [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]

Lymphocytic: Referring to lymphocytes, a type of white blood cell. [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]

Macronutrients: Nutrients in the diet that are the key sources of energy, namely protein, fat, and carbohydrates. [NIH]

Macrophage: A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells. [NIH]

Magnetic Resonance Angiography: Non-invasive method of vascular imaging and determination of internal anatomy without injection of contrast media or radiation exposure. The technique is used especially in cerebral angiography as well as for studies of other vascular structures. [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]

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]

Mammary: Pertaining to the mamma, or breast. [EU]

Mammogram: An x-ray of the breast. [NIH]

Mandible: The largest and strongest bone of the face constituting the lower jaw. It supports the lower teeth. [NIH]

Manic: Affected with mania. [EU]

Marital Status: A demographic parameter indicating a person's status with respect to marriage, divorce, widowhood, singleness, etc. [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]

Meat: The edible portions of any animal used for food including domestic mammals (the major ones being cattle, swine, and sheep) along with poultry, fish, shellfish, and game. [NIH]

Meat Products: Articles of food which are derived by a process of manufacture from any portion of carcasses of any animal used for food (e.g., head cheese, sausage, scrapple). [NIH]

Medial: Lying near the midsaggital plane of the body; opposed to lateral. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

Medical Records: Recording of pertinent information concerning patient's illness or illnesses. [NIH]

Medicament: A medicinal substance or agent. [EU]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Megakaryocytes: Very large bone marrow cells which release mature blood platelets. [NIH]

Megaloblastic: A large abnormal red blood cell appearing in the blood in pernicious anaemia. [EU]

Melanin: The substance that gives the skin its color. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

Membrane Lipids: Lipids, predominantly phospholipids, cholesterol and small amounts of glycolipids found in membranes including cellular and intracellular membranes. These lipids may be arranged in bilayers in the membranes with integral proteins between the layers and peripheral proteins attached to the outside. Membrane lipids are required for active transport, several enzymatic activities and membrane formation. [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]

Menopause: Permanent cessation of menstruation. [NIH]

Menstruation: The normal physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus. [NIH]

Mental: Pertaining to the mind; psychic. 2. (L. mentum chin) pertaining to the chin. [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]

Mental Processes: Conceptual functions or thinking in all its forms. [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]

Mercury: A silver metallic element that exists as a liquid at room temperature. It has the atomic symbol Hg (from hydrargyrum, liquid silver), atomic number 80, and atomic weight 200.59. Mercury is used in many industrial applications and its salts have been employed therapeutically as purgatives, antisyphilitics, disinfectants, and astringents. It can be absorbed through the skin and mucous membranes which leads to mercury poisoning. Because of its toxicity, the clinical use of mercury and mercurials is diminishing. [NIH]

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]

Mesentery: A layer of the peritoneum which attaches the abdominal viscera to the abdominal wall and conveys their blood vessels and nerves. [NIH]

Mesoderm: The middle germ layer of the embryo. [NIH]

Mesolimbic: Inner brain region governing emotion and drives. [NIH]

Metabolic acidosis: (met-ah-BOL-ik as-id-O-sis): A condition in which the blood is too acidic. It may be caused by severe illness or sepsis (bacteria in the bloodstream). [NIH]

Metabolic disorder: A condition in which normal metabolic processes are disrupted, usually because of a missing enzyme. [NIH]

Metabolite: Any substance produced by metabolism or by a metabolic process. [EU]

Metalloendopeptidases: Endopeptidases which use a metal, normally zinc, in the catalytic mechanism. This group of enzymes is inactivated by metal chelators. EC 3.4.24. [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]

Methionine: A sulfur containing essential amino acid that is important in many body functions. It is a chelating agent for heavy metals. [NIH]

Methylcellulose: Methylester of cellulose. Methylcellulose is used as an emulsifying and suspending agent in cosmetics, pharmaceutics and the chemical industry. It is used therapeutically as a bulk laxative. [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]

Microsomal: Of or pertaining to microsomes : vesicular fragments of endoplasmic reticulum formed after disruption and centrifugation of cells. [EU]

Midazolam: A short-acting compound, water-soluble at pH less than 4 and lipid-soluble at physiological pH. It is a hypnotic-sedative drug with anxiolytic and amnestic properties. It is used for sedation in dentistry, cardiac surgery, endoscopic procedures, as preanesthetic medication, and as an adjunct to local anesthesia. Because of its short duration and cardiorespiratory stability, it is particularly useful in poor-risk, elderly, and cardiac patients. [NIH]

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]

Mineralization: The action of mineralizing; the state of being mineralized. [EU]

Mitochondria: Parts of a cell where aerobic production (also known as cell respiration) takes place. [NIH]

Mitochondrial Swelling: Increase in volume of mitochondria due to an influx of fluid; it occurs in hypotonic solutions due to osmotic pressure and in isotonic solutions as a result of altered permeability of the membranes of respiring mitochondria. [NIH]

Mitogen-Activated Protein Kinase Kinases: A serine-threonine protein kinase family whose members are components in protein kinase cascades activated by diverse stimuli. These MAPK kinases phosphorylate mitogen-activated protein kinases and are themselves phosphorylated by MAP kinase kinase kinases. JNK kinases (also known as SAPK kinases) are a subfamily. EC 2.7.10.- [NIH]

Mitogen-Activated Protein Kinases: A superfamily of protein-serine-threonine kinases that are activated by diverse stimuli via protein kinase cascades. They are the final components of the cascades, activated by phosphorylation by mitogen-activated protein kinase kinases which in turn are activated by mitogen-activated protein kinase kinase kinases (MAP kinase kinase kinases). Families of these mitogen-activated protein kinases (MAPKs) include extracellular signal-regulated kinases (ERKs), stress-activated protein kinases (SAPKs) (also known as c-jun terminal kinases (JNKs)), and p38-mitogen-activated protein kinases. EC 2,7,1.- [NIH]

Mitosis: A method of indirect cell division by means of which the two daughter nuclei normally receive identical complements of the number of chromosomes of the somatic cells of the species. [NIH]

Mobility: Capability of movement, of being moved, or of flowing freely. [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]

Modulator: A specific inductor that brings out characteristics peculiar to a definite region. [EU]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Molecular Structure: The location of the atoms, groups or ions relative to one another in a molecule, as well as the number, type and location of covalent bonds. [NIH]

Molecule: A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

Monitor: An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

Monoclonal: An antibody produced by culturing a single type of cell. It therefore consists of a single species of immunoglobulin molecules. [NIH]

Monocyte: A type of white blood cell. [NIH]

Monocyte Chemoattractant Protein-1: A chemokine that is a chemoattractant for human monocytes and may also cause cellular activation of specific functions related to host defense. It is produced by leukocytes of both monocyte and lymphocyte lineage and by fibroblasts during tissue injury. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Monotherapy: A therapy which uses only one drug. [EU]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Mucus: The viscous secretion of mucous membranes. It contains mucin, white blood cells, water, inorganic salts, and exfoliated cells. [NIH]

Multicenter study: A clinical trial that is carried out at more than one medical institution. [NIH]

Multiple Myeloma: A malignant tumor of plasma cells usually arising in the bone marrow; characterized by diffuse involvement of the skeletal system, hyperglobulinemia, Bence-Jones proteinuria, and anemia. [NIH]

Muscular Dystrophies: A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

Mutagenesis: Process of generating genetic mutations. It may occur spontaneously or be induced by mutagens. [NIH]

Mutagenic: Inducing genetic mutation. [EU]

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]

Mycosis: Any disease caused by a fungus. [EU]

Mycosis Fungoides: A chronic malignant T-cell lymphoma of the skin. In the late stages the lymph nodes and viscera are affected. [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]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myopathy: Any disease of a muscle. [EU]

Myosin: Chief protein in muscle and the main constituent of the thick filaments of muscle fibers. In conjunction with actin, it is responsible for the contraction and relaxation of muscles. [NIH]

N-acetyl: Analgesic agent. [NIH]

N-acetyl cysteine: An antioxidant drug that may keep cancer cells from developing or reduce the risk of growth of existing cancer. [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]

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]

Neonatal: Pertaining to the first four weeks after birth. [EU]

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]

Nephrology: A subspecialty of internal medicine concerned with the anatomy, physiology, and pathology of the kidney. [NIH]

Nephropathy: Disease of the kidneys. [EU]

Nephrosis: Descriptive histopathologic term for renal disease without an inflammatory component. [NIH]

Nephrotic: Pertaining to, resembling, or caused by nephrosis. [EU]

Nephrotic Syndrome: Clinical association of heavy proteinuria, hypoalbuminemia, and generalized edema. [NIH]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

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]

Neural tube defects: These defects include problems stemming from fetal development of the spinal cord, spine, brain, and skull, and include birth defects such as spina bifida,

anencephaly, and encephalocele. Neural tube defects occur early in pregnancy at about 4 to 6 weeks, usually before a woman knows she is pregnant. Many babies with neural tube defects have difficulty walking and with bladder and bowel control. [NIH]

Neuroleptic: A term coined to refer to the effects on cognition and behaviour of antipsychotic drugs, which produce a state of apathy, lack of initiative, and limited range of emotion and in psychotic patients cause a reduction in confusion and agitation and normalization of psychomotor activity. [EU]

Neurologic: Having to do with nerves or the nervous system. [NIH]

Neuronal: Pertaining to a neuron or neurons (= conducting cells of the nervous system). [EU]

Neurons: The basic cellular units of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system. [NIH]

Neuropathy: A problem in any part of the nervous system except the brain and spinal cord. Neuropathies can be caused by infection, toxic substances, or disease. [NIH]

Neuropeptide: A member of a class of protein-like molecules made in the brain. Neuropeptides consist of short chains of amino acids, with some functioning as neurotransmitters and some functioning as hormones. [NIH]

Neurosecretory Systems: A system of neurons that has the specialized function to produce and secrete hormones, and that constitutes, in whole or in part, an endocrine organ or system. [NIH]

Neurotensin: A biologically active tridecapeptide isolated from the hypothalamus. It has been shown to induce hypotension in the rat, to stimulate contraction of guinea pig ileum and rat uterus, and to cause relaxation of rat duodenum. There is also evidence that it acts as both a peripheral and a central nervous system neurotransmitter. [NIH]

Neurotoxic: Poisonous or destructive to nerve tissue. [EU]

Neurotoxicity: The tendency of some treatments to cause damage to the nervous system. [NIH]

Neurotransmitter: Any of a group of substances that are released on excitation from the axon terminal of a presynaptic neuron of the central or peripheral nervous system and travel across the synaptic cleft to either excite or inhibit the target cell. Among the many substances that have the properties of a neurotransmitter are acetylcholine, norepinephrine, epinephrine, dopamine, glycine, y-aminobutyrate, glutamic acid, substance P, enkephalins, endorphins, and serotonin. [EU]

Neutrons: Electrically neutral elementary particles found in all atomic nuclei except light hydrogen; the mass is equal to that of the proton and electron combined and they are unstable when isolated from the nucleus, undergoing beta decay. Slow, thermal, epithermal, and fast neutrons refer to the energy levels with which the neutrons are ejected from heavier nuclei during their decay. [NIH]

Neutropenia: An abnormal decrease in the number of neutrophils, a type of white blood cell. [NIH]

Neutrophils: Granular leukocytes having a nucleus with three to five lobes connected by slender threads of chromatin, and cytoplasm containing fine inconspicuous granules and stainable by neutral dyes. [NIH]

Niacin: Water-soluble vitamin of the B complex occurring in various animal and plant tissues. Required by the body for the formation of coenzymes NAD and NADP. Has pellagra-curative, vasodilating, and antilipemic properties. [NIH]

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]

Norepinephrine: Precursor of epinephrine that is secreted by the adrenal medulla and is a widespread central and autonomic neurotransmitter. Norepinephrine is the principal transmitter of most postganglionic sympathetic fibers and of the diffuse projection system in the brain arising from the locus ceruleus. It is also found in plants and is used pharmacologically as a sympathomimetic. [NIH]

Normotensive: 1. Characterized by normal tone, tension, or pressure, as by normal blood pressure. 2. A person with normal blood pressure. [EU]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

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]

Nutritive Value: An indication of the contribution of a food to the nutrient content of the diet. This value depends on the quantity of a food which is digested and absorbed and the amounts of the essential nutrients (protein, fat, carbohydrate, minerals, vitamins) which it contains. This value can be affected by soil and growing conditions, handling and storage, and processing. [NIH]

Nystagmus: An involuntary, rapid, rhythmic movement of the eyeball, which may be horizontal, vertical, rotatory, or mixed, i.e., of two varieties. [EU]

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]

Obsession: A recurrent, persistent thought, image, or impulse that is unwanted and

distressing (ego-dystonic) and comes involuntarily to mind despite attempts to ignore or suppress it. Common obsessions involve thoughts of violence, contamination, and self-doubt. [EU]

Oliguria: Clinical manifestation of the urinary system consisting of a decrease in the amount of urine secreted. [NIH]

Opacity: Degree of density (area most dense taken for reading). [NIH]

Oral Health: The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [NIH]

Organ Preservation: The process by which organs are kept viable outside of the organism from which they were removed (i.e., kept from decay by means of a chemical agent, cooling, or a fluid substitute that mimics the natural state within the organism). [NIH]

Orlistat: A lipase inhibitor used for weight loss. Lipase is an enzyme found in the bowel that assists in lipid absorption by the body. Orlistat blocks this enzyme, reducing the amount of fat the body absorbs by about 30 percent. It is known colloquially as a "fat blocker." Because more oily fat is left in the bowel to be excreted, Orlistat can cause an oily anal leakage and fecal incontinence. Orlistat may not be suitable for people with bowel conditions such as irritable bowel syndrome or Crohn's disease. [NIH]

Orthostatic: Pertaining to or caused by standing erect. [EU]

Osmotic: Pertaining to or of the nature of osmosis (= the passage of pure solvent from a solution of lesser to one of greater solute concentration when the two solutions are separated by a membrane which selectively prevents the passage of solute molecules, but is permeable to the solvent). [EU]

Osteoarthritis: A progressive, degenerative joint disease, the most common form of arthritis, especially in older persons. The disease is thought to result not from the aging process but from biochemical changes and biomechanical stresses affecting articular cartilage. In the foreign literature it is often called osteoarthrosis deformans. [NIH]

Osteoblasts: Bone-forming cells which secrete an extracellular matrix. Hydroxyapatite crystals are then deposited into the matrix to form bone. [NIH]

Osteoclasts: A large multinuclear cell associated with the absorption and removal of bone. An odontoclast, also called cementoclast, is cytomorphologically the same as an osteoclast and is involved in cementum resorption. [NIH]

Osteolytic: Causing the breakdown of bone. [NIH]

Osteoporosis: Reduction of bone mass without alteration in the composition of bone, leading to fractures. Primary osteoporosis can be of two major types: postmenopausal osteoporosis and age-related (or senile) osteoporosis. [NIH]

Ovarian Follicle: Spheroidal cell aggregation in the ovary containing an ovum. It consists of an external fibro-vascular coat, an internal coat of nucleated cells, and a transparent, albuminous fluid in which the ovum is suspended. [NIH]

Ovariectomy: The surgical removal of one or both ovaries. [NIH]

Ovaries: The pair of female reproductive glands in which the ova, or eggs, are formed. The ovaries are located in the pelvis, one on each side of the uterus. [NIH]

Ovary: Either of the paired glands in the female that produce the female germ cells and secrete some of the female sex hormones. [NIH]

Overdose: An accidental or deliberate dose of a medication or street drug that is in excess of what is normally used. [NIH]

Overexpress: An excess of a particular protein on the surface of a cell. [NIH]

Overweight: An excess of body weight but not necessarily body fat; a body mass index of 25 to 29.9 kg/m2. [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]

Ovum Implantation: Endometrial implantation of the blastocyst. [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]

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]

Pancreatectomy: Surgery to remove the pancreas. In a total pancreatectomy, a portion of the stomach, the duodenum, common bile duct, gallbladder, spleen, and nearby lymph nodes also are removed. [NIH]

Pancreatic: Having to do with the pancreas. [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]

Parasite: An animal or a plant that lives on or in an organism of another species and gets at least some of its nutrition from that other organism. [NIH]

Parasitic: Having to do with or being a parasite. A parasite is an animal or a plant that lives on or in an organism of another species and gets at least some of its nutrients from it. [NIH]

Parenteral: Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, etc. [EU]

Parenteral Nutrition: The administering of nutrients for assimilation and utilization by a patient who cannot maintain adequate nutrition by enteral feeding alone. Nutrients are administered by a route other than the alimentary canal (e.g., intravenously, subcutaneously). [NIH]

Parkinsonism: A group of neurological disorders characterized by hypokinesia, tremor, and muscular rigidity. [EU]

Paroxysmal: Recurring in paroxysms (= spasms or seizures). [EU]

Partial remission: The shrinking, but not complete disappearance, of a tumor in response to therapy. Also called partial response. [NIH]

Partial response: A decrease in the size of a tumor, or in the extent of cancer in the body, in response to treatment. [NIH]

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]

Pathogen: Any disease-producing microorganism. [EU]

Pathogenesis: The cellular events and reactions that occur in the development of disease. [NIH]

Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

Pathologist: A doctor who identifies diseases by studying cells and tissues under a microscope. [NIH]

Pathophysiology: Altered functions in an individual or an organ due to disease. [NIH]

Patient Compliance: Voluntary cooperation of the patient in following a prescribed regimen. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Pelvis: The lower part of the abdomen, located between the hip bones. [NIH]

Penicillin: An antibiotic drug used to treat infection. [NIH]

Penile Erection: The state of the penis when the erectile tissue becomes filled with blood and causes the penis to become rigid and elevated. [NIH]

Peptic: Pertaining to pepsin or to digestion; related to the action of gastric juices. [EU]

Peptic Ulcer: An ulceration of the mucous membrane of the esophagus, stomach or duodenum, caused by the action of the acid gastric juice. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Peptide Hydrolases: A subclass of enzymes from the hydrolase class that catalyze the hydrolysis of peptide bonds. Exopeptidases and endopeptidases make up the sub-subclasses for this group. EC 3.4. [NIH]

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]

Periodontitis: Inflammation of the periodontal membrane; also called periodontitis simplex. [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]

Peroxidase: A hemeprotein from leukocytes. Deficiency of this enzyme leads to a hereditary disorder coupled with disseminated moniliasis. It catalyzes the conversion of a donor and peroxide to an oxidized donor and water. EC 1.11.1.7. [NIH]

Peroxide: Chemical compound which contains an atom group with two oxygen atoms tied to each other. [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]

Pharmaceutic Aids: Substances which are of little or no therapeutic value, but are necessary in the manufacture, compounding, storage, etc., of pharmaceutical preparations or drug dosage forms. They include solvents, diluting agents, and suspending agents, and emulsifying agents. Also, antioxidants; preservatives, pharmaceutical; dyes (coloring agents); flavoring agents; vehicles; excipients; ointment bases. [NIH]

Pharmaceutical Preparations: Drugs intended for human or veterinary use, presented in their finished dosage form. Included here are materials used in the preparation and/or formulation of the finished dosage form. [NIH]

Pharmacodynamic: Is concerned with the response of living tissues to chemical stimuli, that is, the action of drugs on the living organism in the absence of disease. [NIH]

Pharmacokinetic: The mathematical analysis of the time courses of absorption, distribution, and elimination of drugs. [NIH]

Pharmacologic: Pertaining to pharmacology or to the properties and reactions of drugs. [EU]

Pharmacotherapy: A regimen of using appetite suppressant medications to manage obesity by decreasing appetite or increasing the feeling of satiety. These medications decrease appetite by increasing serotonin or catecholamine—two brain chemicals that affect mood and appetite. [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]

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]

Physicochemical: Pertaining to physics and chemistry. [EU]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Physiology: The science that deals with the life processes and functions of organismus, their cells, tissues, and organs. [NIH]

Pilot study: The initial study examining a new method or treatment. [NIH]

Pituitary Gland: A small, unpaired gland situated in the sella turcica tissue. It is connected to the hypothalamus by a short stalk. [NIH]

Placenta: A highly vascular fetal organ through which the fetus absorbs oxygen and other nutrients and excretes carbon dioxide and other wastes. It begins to form about the eighth day of gestation when the blastocyst adheres to the decidua. [NIH]

Plants: Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

Plaque: A clear zone in a bacterial culture grown on an agar plate caused by localized destruction of bacterial cells by a bacteriophage. The concentration of infective virus in a fluid can be estimated by applying the fluid to a culture and counting the number of. [NIH]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

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]

Plasmapheresis: Procedure whereby plasma is separated and extracted from anticoagulated whole blood and the red cells retransfused to the donor. Plasmapheresis is also employed for therapeutic use. [NIH]

Plasmin: A product of the lysis of plasminogen (profibrinolysin) by plasminogen activators. It is composed of two polypeptide chains, light (B) and heavy (A), with a molecular weight of 75,000. It is the major proteolytic enzyme involved in blood clot retraction or the lysis of fibrin and quickly inactivated by antiplasmins. EC 3.4.21.7. [NIH]

Plasminogen: Precursor of fibrinolysin (plasmin). It is a single-chain beta-globulin of molecular weight 80-90,000 found mostly in association with fibrinogen in plasma; plasminogen activators change it to fibrinolysin. It is used in wound debriding and has been investigated as a thrombolytic agent. [NIH]

Plasminogen Activators: A heterogeneous group of proteolytic enzymes that convert plasminogen to plasmin. They are concentrated in the lysosomes of most cells and in the vascular endothelium, particularly in the vessels of the microcirculation. EC 3.4.21.-. [NIH]

Platelet Activating Factor: A phospholipid derivative formed by platelets, basophils, neutrophils, monocytes, and macrophages. It is a potent platelet aggregating agent and inducer of systemic anaphylactic symptoms, including hypotension, thrombocytopenia, neutropenia, and bronchoconstriction. [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]

Plateletpheresis: The preparation of platelet concentrates with the return of red cells and platelet-poor plasma to the donor. [NIH]

Platelets: A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called thrombocytes. [NIH]

Pneumonectomy: An operation to remove an entire lung. [NIH]

Pneumonia: Inflammation of the lungs. [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]

Polyarthritis: An inflammation of several joints together. [EU]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand

as a template. The polymerase copies the template in the 5'-3'direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

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]

Polyposis: The development of numerous polyps (growths that protrude from a mucous membrane). [NIH]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Polyunsaturated fat: An unsaturated fat found in greatest amounts in foods derived from plants, including safflower, sunflower, corn, and soybean oils. [NIH]

Portal Hypertension: High blood pressure in the portal vein. This vein carries blood into the liver. Portal hypertension is caused by a blood clot. This is a common complication of cirrhosis. [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]

Postprandial: Occurring after dinner, or after a meal; postcibal. [EU]

Potentiating: A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [NIH]

Potentiation: An overall effect of two drugs taken together which is greater than the sum of the effects of each drug taken alone. [NIH]

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]

Pravastatin: An antilipemic fungal metabolite isolated from cultures of Nocardia autotrophica. It acts as a competitive inhibitor of HMG CoA reductase (hydroxymethylglutaryl CoA reductases). [NIH]

Precipitation: The act or process of precipitating. [EU]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Predisposition: A latent susceptibility to disease which may be activated under certain conditions, as by stress. [EU]

Prednisolone: A glucocorticoid with the general properties of the corticosteroids. It is the drug of choice for all conditions in which routine systemic corticosteroid therapy is indicated, except adrenal deficiency states. [NIH]

Prednisone: A synthetic anti-inflammatory glucocorticoid derived from cortisone. It is biologically inert and converted to prednisolone in the liver. [NIH]

Preoperative: Preceding an operation. [EU]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Primary Biliary Cirrhosis: A chronic liver disease. Slowly destroys the bile ducts in the liver. This prevents release of bile. Long-term irritation of the liver may cause scarring and cirrhosis in later stages of the disease. [NIH]

Primary Prevention: Prevention of disease or mental disorders in susceptible individuals or populations through promotion of health, including mental health, and specific protection, as in immunization, as distinguished from the prevention of complications or after-effects of existing disease. [NIH]

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]

Problem Solving: A learning situation involving more than one alternative from which a selection is made in order to attain a specific goal. [NIH]

Prodrug: A substance that gives rise to a pharmacologically active metabolite, although not itself active (i. e. an inactive precursor). [NIH]

Progesterone: Pregn-4-ene-3,20-dione. The principal progestational hormone of the body, secreted by the corpus luteum, adrenal cortex, and placenta. Its chief function is to prepare the uterus for the reception and development of the fertilized ovum. It acts as an antiovulatory agent when administered on days 5-25 of the menstrual cycle. [NIH]

Progression: Increase in the size of a tumor or spread of cancer in the body. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Proinsulin: The substance made first in the pancreas that is then made into insulin. When insulin is purified from the pancreas of pork or beef, all the proinsulin is not fully removed. When some people use these insulins, the proinsulin can cause the body to react with a rash, to resist the insulin, or even to make dents or lumps in the skin at the place where the insulin is injected. The purified insulins have less proinsulin and other impurities than the other types of insulins. [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]

Prone: Having the front portion of the body downwards. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Propranolol: A widely used non-cardioselective beta-adrenergic antagonist. Propranolol is used in the treatment or prevention of many disorders including acute myocardial infarction, arrhythmias, angina pectoris, hypertension, hypertensive emergencies, hyperthyroidism, migraine, pheochromocytoma, menopause, and anxiety. [NIH]

Prospective study: An epidemiologic study in which a group of individuals (a cohort), all

free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

Prostaglandins: A group of compounds derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway. They are extremely potent mediators of a diverse group of physiological processes. [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 Binding: The process in which substances, either endogenous or exogenous, bind to proteins, peptides, enzymes, protein precursors, or allied compounds. Specific protein-binding measures are often used as assays in diagnostic assessments. [NIH]

Protein C: A vitamin-K dependent zymogen present in the blood, which, upon activation by thrombin and thrombomodulin exerts anticoagulant properties by inactivating factors Va and VIIIa at the rate-limiting steps of thrombin formation. [NIH]

Protein 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 Kinase C: An enzyme that phosphorylates proteins on serine or threonine residues in the presence of physiological concentrations of calcium and membrane phospholipids. The additional presence of diacylglycerols markedly increases its sensitivity to both calcium and phospholipids. The sensitivity of the enzyme can also be increased by phorbol esters and it is believed that protein kinase C is the receptor protein of tumor-promoting phorbol esters. EC 2.7.1.-. [NIH]

Protein 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]

Protein-Serine-Threonine Kinases: A group of enzymes that catalyzes the phosphorylation of serine or threonine residues in proteins, with ATP or other nucleotides as phosphate donors. EC 2.7.10. [NIH]

Proteinuria: The presence of protein in the urine, indicating that the kidneys are not working properly. [NIH]

Proteoglycan: A molecule that contains both protein and glycosaminoglycans, which are a type of polysaccharide. Proteoglycans are found in cartilage and other connective tissues. [NIH]

Proteolytic: 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Proteome: The protein complement of an organism coded for by its genome. [NIH]

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]

Pruritus: An intense itching sensation that produces the urge to rub or scratch the skin to obtain relief. [NIH]

Psychiatric: Pertaining to or within the purview of psychiatry. [EU]

Psychiatry: The medical science that deals with the origin, diagnosis, prevention, and treatment of mental disorders. [NIH]

Psychoactive: Those drugs which alter sensation, mood, consciousness or other psychological or behavioral functions. [NIH]

Psychology: The science dealing with the study of mental processes and behavior in man and animals. [NIH]

Psychosis: A mental disorder characterized by gross impairment in reality testing as evidenced by delusions, hallucinations, markedly incoherent speech, or disorganized and agitated behaviour without apparent awareness on the part of the patient of the incomprehensibility of his behaviour; the term is also used in a more general sense to refer to mental disorders in which mental functioning is sufficiently impaired as to interfere grossly with the patient's capacity to meet the ordinary demands of life. Historically, the term has been applied to many conditions, e.g. manic-depressive psychosis, that were first described in psychotic patients, although many patients with the disorder are not judged psychotic. [EU]

Public Health: Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the international, national, state, or municipal level. [NIH]

Public Policy: A course or method of action selected, usually by a government, from among alternatives to guide and determine present and future decisions. [NIH]

Publishing: "The business or profession of the commercial production and issuance of literature" (Webster's 3d). It includes the publisher, publication processes, editing and editors. Production may be by conventional printing methods or by electronic publishing. [NIH]

Pulmonary: Relating to the lungs. [NIH]

Pulmonary Artery: The short wide vessel arising from the conus arteriosus of the right ventricle and conveying unaerated blood to the lungs. [NIH]

Pulmonary Edema: An accumulation of an excessive amount of watery fluid in the lungs, may be caused by acute exposure to dangerous concentrations of irritant gasses. [NIH]

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]

Purified Insulins: Insulins with much less of the impure proinsulin. It is thought that the use of purified insulins may help avoid or reduce some of the problems of people with

diabetes such as allergic reactions. [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]

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]

Quercetin: Aglucon of quercetrin, rutin, and other glycosides. It is widely distributed in the plant kingdom, especially in rinds and barks, clover blossoms, and ragweed pollen. [NIH]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

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]

Radiolabeled: Any compound that has been joined with a radioactive substance. [NIH]

Radiotherapy: The use of ionizing radiation to treat malignant neoplasms and other benign conditions. The most common forms of ionizing radiation used as therapy are x-rays, gamma rays, and electrons. A special form of radiotherapy, targeted radiotherapy, links a cytotoxic radionuclide to a molecule that targets the tumor. When this molecule is an antibody or other immunologic molecule, the technique is called radioimmunotherapy. [NIH]

Raloxifene: A second generation selective estrogen receptor modulator (SERM) used to prevent osteoporosis in postmenopausal women. It has estrogen agonist effects on bone and cholesterol metabolism but behaves as a complete estrogen antagonist on mammary gland and uterine tissue. [NIH]

Randomized: Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

Randomized clinical trial: A study in which the participants are assigned by chance to separate groups that compare different treatments; neither the researchers nor the participants can choose which group. Using chance to assign people to groups means that the groups will be similar and that the treatments they receive can be compared objectively. At the time of the trial, it is not known which treatment is best. It is the patient's choice to be in a randomized trial. [NIH]

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]

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]

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]

Reductase: Enzyme converting testosterone to dihydrotestosterone. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

Reference Values: The range or frequency distribution of a measurement in a population (of organisms, organs or things) that has not been selected for the presence of disease or abnormality. [NIH]

Reflux: The term used when liquid backs up into the esophagus from the stomach. [NIH]

Refraction: A test to determine the best eyeglasses or contact lenses to correct a refractive error (myopia, hyperopia, or astigmatism). [NIH]

Refractory: Not readily yielding to treatment. [EU]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Regurgitation: A backward flowing, as the casting up of undigested food, or the backward flowing of blood into the heart, or between the chambers of the heart when a valve is incompetent. [EU]

Rehydration: The restoration of water or of fluid content to a body or to substance which has become dehydrated. [EU]

Reliability: Used technically, in a statistical sense, of consistency of a test with itself, i. e. the extent to which we can assume that it will yield the same result if repeated a second time. [NIH]

Remission: A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although there still may be cancer in the body. [NIH]

Renal Replacement Therapy: Procedures which temporarily or permanently remedy insufficient cleansing of body fluids by the kidneys. [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]

Research Support: Financial support of research activities. [NIH]

Resorption: The loss of substance through physiologic or pathologic means, such as loss of dentin and cementum of a tooth, or of the alveolar process of the mandible or maxilla. [EU]

Respiration: The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

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]

Retinoids: Derivatives of vitamin A. Used clinically in the treatment of severe cystic acne, psoriasis, and other disorders of keratinization. Their possible use in the prophylaxis and treatment of cancer is being actively explored. [NIH]

Retinol: Vitamin A. It is essential for proper vision and healthy skin and mucous membranes. Retinol is being studied for cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Retinopathy: 1. Retinitis (= inflammation of the retina). 2. Retinosis (= degenerative, noninflammatory condition of the retina). [EU]

Retinyl palmitate: A drug being studied in cancer prevention; it belongs to the family of drugs called retinoids. [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]

Reverse Transcriptase Inhibitors: Inhibitors of reverse transcriptase (RNA-directed DNA polymerase), an enzyme that synthesizes DNA on an RNA template. [NIH]

Rhabdomyolysis: Necrosis or disintegration of skeletal muscle often followed by myoglobinuria. [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]

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]

Rickets: A condition caused by deficiency of vitamin D, especially in infancy and childhood, with disturbance of normal ossification. The disease is marked by bending and distortion of the bones under muscular action, by the formation of nodular enlargements on the ends and sides of the bones, by delayed closure of the fontanelles, pain in the muscles, and sweating of the head. Vitamin D and sunlight together with an adequate diet are curative, provided that the parathyroid glands are functioning properly. [EU]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Risk patient: Patient who is at risk, because of his/her behaviour or because of the type of person he/she is. [EU]

Risperidone: A selective blocker of dopamine D2 and serotonin-5-HT-2 receptors that acts as an atypical antipsychotic agent. It has been shown to improve both positive and negative symptoms in the treatment of schizophrenia. [NIH]

Ritonavir: An HIV protease inhibitor that works by interfering with the reproductive cycle of HIV. [NIH]

Rod: A reception for vision, located in the retina. [NIH]

Rosiglitazone: A drug taken to help reduce the amount of sugar in the blood. Rosiglitazone helps make insulin more effective and improves regulation of blood sugar. It belongs to the family of drugs called thiazolidinediones. [NIH]

Rutin: 3-((6-O-(6-Deoxy-alpha-L-mannopyranosyl)-beta-D-glucopyranosyl)oxy)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-1-benzopyran-4-one. Found in many plants, including buckwheat, tobacco, forsythia, hydrangea, pansies, etc. It has been used therapeutically to decrease capillary fragility. [NIH]

Saliva: The clear, viscous fluid secreted by the salivary glands and mucous glands of the mouth. It contains mucins, water, organic salts, and ptylin. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Saphenous: Applied to certain structures in the leg, e. g. nerve vein. [NIH]

Saphenous Vein: The vein which drains the foot and leg. [NIH]

Saponins: Sapogenin glycosides. A type of glycoside widely distributed in plants. Each consists of a sapogenin as the aglycon moiety, and a sugar. The sapogenin may be a steroid or a triterpene and the sugar may be glucose, galactose, a pentose, or a methylpentose. Sapogenins are poisonous towards the lower forms of life and are powerful hemolytics when injected into the blood stream able to dissolve red blood cells at even extreme dilutions. [NIH]

Saturated fat: A type of fat found in greatest amounts in foods from animals, such as fatty cuts of meat, poultry with the skin, whole-milk dairy products, lard, and in some vegetable oils, including coconut, palm kernel, and palm oils. Saturated fat raises blood cholesterol more than anything else eaten. On a Step I Diet, no more than 8 to 10 percent of total calories should come from saturated fat, and in the Step II Diet, less than 7 percent of the day's total calories should come from saturated fat. [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]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

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]

Sedative: 1. Allaying activity and excitement. 2. An agent that allays excitement. [EU]

Selective estrogen receptor modulator: SERM. A drug that acts like estrogen on some tissues, but blocks the effect of estrogen on other tissues. Tamoxifen and raloxifene are SERMs. [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]

Senescence: The bodily and mental state associated with advancing age. [NIH]

Senile: Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

Sepsis: The presence of bacteria in the bloodstream. [NIH]

Sequencing: The determination of the order of nucleotides in a DNA or RNA chain. [NIH]

Serine: A non-essential amino acid occurring in natural form as the L-isomer. It is synthesized from glycine or threonine. It is involved in the biosynthesis of purines, pyrimidines, and other amino acids. [NIH]

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]

Serotonin: A biochemical messenger and regulator, synthesized from the essential amino acid L-tryptophan. In humans it is found primarily in the central nervous system, gastrointestinal tract, and blood platelets. Serotonin mediates several important physiological functions including neurotransmission, gastrointestinal motility, hemostasis, and cardiovascular integrity. Multiple receptor families (receptors, serotonin) explain the broad physiological actions and distribution of this biochemical mediator. [NIH]

Serous: Having to do with serum, the clear liquid part of blood. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Serum Albumin: A major plasma protein that serves in maintaining the plasma colloidal osmotic pressure and transporting large organic anions. [NIH]

Sex Characteristics: Those characteristics that distinguish one sex from the other. The

primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

Shivering: Involuntary contraction or twitching of the muscles. It is a physiologic method of heat production in man and other mammals. [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]

Sicca: Failure of lacrimal secretion, keratoconjunctivitis sicca, failure of secretion of the salivary glands and mucous glands of the upper respiratory tract and polyarthritis. [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]

Simvastatin: A derivative of lovastatin and potent competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase (hydroxymethylglutaryl CoA reductases), which is the rate-limiting enzyme in cholesterol biosynthesis. It may also interfere with steroid hormone production. Due to the induction of hepatic LDL receptors, it increases breakdown of LDL-cholesterol (lipoproteins, LDL cholesterol). [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]

Sleep apnea: A serious, potentially life-threatening breathing disorder characterized by repeated cessation of breathing due to either collapse of the upper airway during sleep or absence of respiratory effort. [NIH]

Sleep Deprivation: The state of being deprived of sleep under experimental conditions, due to life events, or from a wide variety of pathophysiologic causes such as medication effect, chronic illness, psychiatric illness, or sleep disorder. [NIH]

Small intestine: The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

Smooth muscle: Muscle that performs automatic tasks, such as constricting blood vessels. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

Social Support: Support systems that provide assistance and encouragement to individuals with physical or emotional disabilities in order that they may better cope. Informal social support is usually provided by friends, relatives, or peers, while formal assistance is provided by churches, groups, etc. [NIH]

Sodium: An element that is a member of the alkali group of metals. It has the atomic symbol Na, atomic number 11, and atomic weight 23. With a valence of 1, it has a strong affinity for oxygen and other nonmetallic elements. Sodium provides the chief cation of the extracellular body fluids. Its salts are the most widely used in medicine. (From Dorland, 27th ed) Physiologically the sodium ion plays a major role in blood pressure regulation, maintenance of fluid volume, and electrolyte balance. [NIH]

Soft tissue: Refers to muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body. [NIH]

Solid tumor: Cancer of body tissues other than blood, bone marrow, or the lymphatic system. [NIH]

Solvent: 1. Dissolving; effecting a solution. 2. A liquid that dissolves or that is capable of dissolving; the component of a solution that is present in greater amount. [EU]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Soybean Oil: Oil from soybean or soybean plant. [NIH]

Spasm: An involuntary contraction of a muscle or group of muscles. Spasms may involve skeletal muscle or smooth muscle. [NIH]

Spastic: 1. Of the nature of or characterized by spasms. 2. Hypertonic, so that the muscles are stiff and the movements awkward. 3. A person exhibiting spasticity, such as occurs in spastic paralysis or in cerebral palsy. [EU]

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]

Spinal cord: The main trunk or bundle of nerves running down the spine through holes in the spinal bone (the vertebrae) from the brain to the level of the lower back. [NIH]

Spleen: An organ that is part of the lymphatic system. The spleen produces lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach. [NIH]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Stabilization: The creation of a stable state. [EU]

Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

Statistically significant: Describes a mathematical measure of difference between groups. The difference is said to be statistically significant if it is greater than what might be expected to happen by chance alone. [NIH]

Steatosis: Fatty degeneration. [EU]

Steel: A tough, malleable, iron-based alloy containing up to, but no more than, two percent carbon and often other metals. It is used in medicine and dentistry in implants and instrumentation. [NIH]

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]

Stenosis: Narrowing or stricture of a duct or canal. [EU]

Steroid: A group name for lipids that contain a hydrogenated cyclopentanoperhydrophenanthrene ring system. Some of the substances included in this group are progesterone, adrenocortical hormones, the gonadal hormones, cardiac aglycones, bile acids, sterols (such as cholesterol), toad poisons, saponins, and some of the carcinogenic hydrocarbons. [EU]

Stimulus: That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Stool: The waste matter discharged in a bowel movement; feces. [NIH]

Streptococcus: A genus of gram-positive, coccoid bacteria whose organisms occur in pairs or chains. No endospores are produced. Many species exist as commensals or parasites on man or animals with some being highly pathogenic. A few species are saprophytes and occur in the natural environment. [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]

Stricture: The abnormal narrowing of a body opening. Also called stenosis. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Stromal: Large, veil-like cell in the bone marrow. [NIH]

Stromal Cells: Connective tissue cells of an organ found in the loose connective tissue. These are most often associated with the uterine mucosa and the ovary as well as the hematopoietic system and elsewhere. [NIH]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subarachnoid: Situated or occurring between the arachnoid and the pia mater. [EU]

Subclavian: The direct continuation of the axillary vein at the lateral border of the first rib. It passes medially to join the internal jugular vein and form the brachiocephalic vein on each side. [NIH]

Subclavian Vein: The continuation of the axillary vein which follows the subclavian artery and then joins the internal jugular vein to form the brachiocephalic vein. [NIH]

Subclinical: Without clinical manifestations; said of the early stage(s) of an infection or other disease or abnormality before symptoms and signs become apparent or detectable by clinical examination or laboratory tests, or of a very mild form of an infection or other disease or abnormality. [EU]

Subcutaneous: Beneath the skin. [NIH]

Subspecies: A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

Substance P: An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

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]

Suppositories: A small cone-shaped medicament having cocoa butter or gelatin at its basis and usually intended for the treatment of local conditions in the rectum. [NIH]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Surface Plasmon Resonance: A biosensing technique in which biomolecules capable of binding to specific analytes or ligands are first immobilized on one side of a metallic film. Light is then focused on the opposite side of the film to excite the surface plasmons, that is, the oscillations of free electrons propagating along the film's surface. The refractive index of light reflecting off this surface is measured. When the immobilized biomolecules are bound by their ligands, an alteration in surface plasmons on the opposite side of the film is created which is directly proportional to the change in bound, or adsorbed, mass. Binding is measured by changes in the refractive index. The technique is used to study biomolecular interactions, such as antigen-antibody binding. [NIH]

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]

Sympathomimetic: 1. Mimicking the effects of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. 2. An agent that produces effects similar to those of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. Called also adrenergic. [EU]

Symphysis: A secondary cartilaginous joint. [NIH]

Symptomatic: Having to do with symptoms, which are signs of a condition or disease. [NIH]

Synapse: The region where the processes of two neurons come into close contiguity, and the nervous impulse passes from one to the other; the fibers of the two are intermeshed, but, according to the general view, there is no direct contiguity. [NIH]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Systemic: Affecting the entire body. [NIH]

Systemic lupus erythematosus: SLE. A chronic inflammatory connective tissue disease marked by skin rashes, joint pain and swelling, inflammation of the kidneys, inflammation of the fibrous tissue surrounding the heart (i.e., the pericardium), as well as other problems. Not all affected individuals display all of these problems. May be referred to as lupus. [NIH]

Systolic: Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

Systolic blood pressure: The maximum pressure in the artery produced as the heart contracts and blood begins to flow. [NIH]

Tacrolimus: A macrolide isolated from the culture broth of a strain of Streptomyces tsukubaensis that has strong immunosuppressive activity in vivo and prevents the activation of T-lymphocytes in response to antigenic or mitogenic stimulation in vitro. [NIH]

Tardive: Marked by lateness, late; said of a disease in which the characteristic lesion is late in appearing. [EU]

Testis: Either of the paired male reproductive glands that produce the male germ cells and the male hormones. [NIH]

Testosterone: A hormone that promotes the development and maintenance of male sex characteristics. [NIH]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thermogenesis: The generation of heat in order to maintain body temperature. The uncoupled oxidation of fatty acids contained within brown adipose tissue and shivering are examples of thermogenesis in mammals. [NIH]

Thigh: A leg; in anatomy, any elongated process or part of a structure more or less comparable to a leg. [NIH]

Thorax: A part of the trunk between the neck and the abdomen; the chest. [NIH]

Threshold: For a specified sensory modality (e. g. light, sound, vibration), the lowest level (absolute threshold) or smallest difference (difference threshold, difference limen) or intensity of the stimulus discernible in prescribed conditions of stimulation. [NIH]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombocytes: Blood cells that help prevent bleeding by causing blood clots to form. Also called platelets. [NIH]

Thrombocytopenia: A decrease in the number of blood platelets. [NIH]

Thrombolytic: 1. Dissolving or splitting up a thrombus. 2. A thrombolytic agent. [EU]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thrombus: An aggregation of blood factors, primarily platelets and fibrin with entrapment of cellular elements, frequently causing vascular obstruction at the point of its formation. Some authorities thus differentiate thrombus formation from simple coagulation or clot formation. [EU]

Thymus: An organ that is part of the lymphatic system, in which T lymphocytes grow and multiply. The thymus is in the chest behind the breastbone. [NIH]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [NIH]

Thyroid Gland: A highly vascular endocrine gland consisting of two lobes, one on either side of the trachea, joined by a narrow isthmus; it produces the thyroid hormones which are concerned in regulating the metabolic rate of the body. [NIH]

Thyroxine: An amino acid of the thyroid gland which exerts a stimulating effect on thyroid metabolism. [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]

Tone: 1. The normal degree of vigour and tension; in muscle, the resistance to passive

elongation or stretch; tonus. 2. A particular quality of sound or of voice. 3. To make permanent, or to change, the colour of silver stain by chemical treatment, usually with a heavy metal. [EU]

Tonus: A state of slight tension usually present in muscles even when they are not undergoing active contraction. [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]

Total pancreatectomy: Surgery to remove the entire pancreas. [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]

Toxicokinetics: Study of the absorption, distribution, metabolism, and excretion of test substances. [NIH]

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]

Toxin: A poison; frequently used to refer specifically to a protein produced by some higher plants, certain animals, and pathogenic bacteria, which is highly toxic for other living organisms. Such substances are differentiated from the simple chemical poisons and the vegetable alkaloids by their high molecular weight and antigenicity. [EU]

Trace element: Substance or element essential to plant or animal life, but present in extremely small amounts. [NIH]

Traction: The act of pulling. [NIH]

Transcriptase: An enzyme which catalyses the synthesis of a complementary mRNA molecule from a DNA template in the presence of a mixture of the four ribonucleotides (ATP, UTP, GTP and CTP). [NIH]

Transcription Factors: Endogenous substances, usually proteins, which are effective in the initiation, stimulation, or termination of the genetic transcription process. [NIH]

Transdermal: Entering through the dermis, or skin, as in administration of a drug applied to the skin in ointment or patch form. [EU]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

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]

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]

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]

Tricyclic: Containing three fused rings or closed chains in the molecular structure. [EU]

Trigger zone: Dolorogenic zone (= producing or causing pain). [EU]

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]

Trivalent: Having a valence of three. [EU]

Troglitazone: A drug used in diabetes treatment that is being studied for its effect on reducing the risk of cancer cell growth in fat tissue. [NIH]

Trophoblast: The outer layer of cells of the blastocyst which works its way into the endometrium during ovum implantation and grows rapidly, later combining with mesoderm. [NIH]

Truncal: The bilateral dissection of the abdominal branches of the vagus nerve. [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]

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 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]

Tungsten: A metallic element with the atomic symbol W, atomic number 74, and atomic weight 183.85. It is used in many manufacturing applications, including increasing the hardness, toughness, and tensile strength of steel; manufacture of filaments for incandescent light bulbs; and in contact points for automotive and electrical apparatus. [NIH]

Tungsten Compounds: Inorganic compounds that contain tungsten as an integral part of the molecule. [NIH]

Tunica: A rather vague term to denote the lining coat of hollow organs, tubes, or cavities. [NIH]

Type 2 diabetes: Usually characterized by a gradual onset with minimal or no symptoms of metabolic disturbance and no requirement for exogenous insulin. The peak age of onset is 50 to 60 years. Obesity and possibly a genetic factor are usually present. [NIH]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

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]

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]

Urease: An enzyme that catalyzes the conversion of urea and water to carbon dioxide and ammonia. EC 3.5.1.5. [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]

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]

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]

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]

Vaccines: Suspensions of killed or attenuated microorganisms (bacteria, viruses, fungi, protozoa, or rickettsiae), antigenic proteins derived from them, or synthetic constructs, administered for the prevention, amelioration, or treatment of infectious and other diseases. [NIH]

Vagina: The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

Vaginal: Of or having to do with the vagina, the birth canal. [NIH]

Vaginosis: A condition caused by the overgrowth of anaerobic bacteria (e. g., Gardnerella vaginalis), resulting in vaginal irritation and discharge. [NIH]

Vagus Nerve: The 10th cranial nerve. The vagus is a mixed nerve which contains somatic afferents (from skin in back of the ear and the external auditory meatus), visceral afferents (from the pharynx, larynx, thorax, and abdomen), parasympathetic efferents (to the thorax and abdomen), and efferents to striated muscle (of the larynx and pharynx). [NIH]

Valves: Flap-like structures that control the direction of blood flow through the heart. [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]

Vasculitis: Inflammation of a blood vessel. [NIH]

Vasodilation: Physiological dilation of the blood vessels without anatomic change. For dilation with anatomic change, dilatation, pathologic or aneurysm (or specific aneurysm) is

used. [NIH]

Vasodilators: Any nerve or agent which induces dilatation of the blood vessels. [NIH]

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]

Ventricle: One of the two pumping chambers of the heart. The right ventricle receives oxygen-poor blood from the right atrium and pumps it to the lungs through the pulmonary artery. The left ventricle receives oxygen-rich blood from the left atrium and pumps it to the body through the aorta. [NIH]

Ventricular: Pertaining to a ventricle. [EU]

Venules: The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

Vertigo: An illusion of movement; a sensation as if the external world were revolving around the patient (objective vertigo) or as if he himself were revolving in space (subjective vertigo). The term is sometimes erroneously used to mean any form of dizziness. [EU]

Very low-density lipoprotein: The lipoprotein particles that initially leave the liver, carrying cholesterol and lipid. VLDLs contain 10 to 15 percent of the total serum cholesterol along with most of the triglycerides in the fasting serum; VLDLs are precursors of LDL, and some forms of VLDL, particularly VLDL remnants, appear to be atherogenic. [NIH]

Vesicular: 1. Composed of or relating to small, saclike bodies. 2. Pertaining to or made up of vesicles on the skin. [EU]

Vestibular: Pertaining to or toward a vestibule. In dental anatomy, used to refer to the tooth surface directed toward the vestibule of the mouth. [EU]

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]

Viral Load: The quantity of measurable virus in the blood. Change in viral load, measured in plasma, is used as a surrogate marker in HIV disease progression. [NIH]

Virulence: The degree of pathogenicity within a group or species of microorganisms or viruses as indicated by case fatality rates and/or the ability of the organism to invade the tissues of the host. [NIH]

Virus: Submicroscopic organism that causes infectious disease. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

Virus Diseases: A general term for diseases produced by viruses. [NIH]

Viscera: Any of the large interior organs in any one of the three great cavities of the body, especially in the abdomen. [NIH]

Visceral: , from viscus a viscus) pertaining to a viscus. [EU]

Visceral fat: One of the three compartments of abdominal fat. Retroperitoneal and subcutaneous are the other two compartments. [NIH]

Vitamin A: A substance used in cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Vitamin D: The vitamin that mediates intestinal calcium absorption, bone calcium metabolism, and probably muscle activity. It usually acts as a hormone precursor, requiring

2 stages of metabolism before reaching actual hormonal form. It is isolated from fish liver oils and used in the treatment and prevention of rickets. [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]

White blood cell: A type of cell in the immune system that helps the body fight infection and disease. White blood cells include lymphocytes, granulocytes, macrophages, and others. [NIH]

Withdrawal: 1. A pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality disorders. 2. (DSM III-R) A substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

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]

Xanthine: An urinary calculus. [NIH]

Xanthine Oxidase: An iron-molybdenum flavoprotein containing FAD that oxidizes hypoxanthine, some other purines and pterins, and aldehydes. Deficiency of the enzyme, an autosomal recessive trait, causes xanthinuria. EC 1.1.3.22. [NIH]

Xanthoma: A tumour composed of lipid-laden foam cells, which are histiocytes containing cytoplasmic lipid material. Called also xanthelasma. [EU]

Xanthomatosis: A condition of morphologic change in which there is accumulation of lipids in the large foam cells of tissues. It is the cutaneous manifestation of lipidosis in which plasma fatty acids and lipoproteins are quantitatively changed. The xanthomatous eruptions have several different distinct morphologies dependent upon the specific form taken by the disease. [NIH]

Xenograft: The cells of one species transplanted to another species. [NIH]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [NIH]

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]

INDEX

B

C

F

N

Q

R

S


9 780497 005689