KIDNEY DISEASE

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

JAMES N. PARKER, M.D.
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About the Editors

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FORWARD

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

The Editors

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

CHAPTER 1. STUDIES ON KIDNEY DISEASE

Overview

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

The Combined Health Information Database

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

- **Kidney Disease and Gastrointestinal Involvement**

  Source: Dialysis and Transplantation. 29(4): 202-204, 206-207. April 2000.

  Contact: Available from Dialysis and Transplantation, Attn.: Subscriptions. P.O. Box 10535, Riverton, NJ 08076. (800) 624-4196 or (609) 786-0871.

  Summary: Some kidney diseases may present with gastrointestinal (GI) manifestations. Conversely, in some GI diseases, renal involvement is present. In addition, some systemic diseases are associated with both kidney and GI involvement. In this review article, the interrelationship between kidney diseases and GI manifestations is addressed. The interrelationship between the kidney and liver diseases is also covered. Patients with chronic renal failure often consult a gastroenterologist first because of anorexia, nausea, vomiting, heartburn, and indigestion of a few month's duration.

Patients with acute renal failure may also present with anorexia (lack of appetite), nausea, vomiting, and GI bleeding. Kidney diseases that may cause GI manifestations include acute glomerulonephritis, nephrotic syndrome, reflux nephropathy and pyelonephritis, analgesic (pain medication) nephropathy, acute tubulointerstitial nephritis following administration of NSAIDs, obstructive uropathy, polycystic kidney disease, and GI manifestations in patients on dialysis. GI related causes may contribute to the following kidney diseases: prerenal failure, resulting from fluid losses related to vomiting, diarrhea, hemorrhage, bowel fistula, or bowel obstruction; acute tubular necrosis, resulting from extreme renal ischemia; obstructive uropathy, usually due to active inflammatory GI disease; urinary tract infections, which often result in women from E. coli ascending from the GI tract; postinfectious glomerulonephritis; IgA nephropathy, which is often secondary to chronic liver diseases, celiac disease (gluten intolerance), Crohn's disease, adenocarcinomas of the GI tract; and liver disease. 23 references.

- **6 Ways to Beat Kidney Disease**

  Source: Diabetes Forecast. 52(3): 56-58. March 1999.

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

  Summary: This article discusses the occurrence and prevention of kidney disease in people who have diabetes. Diabetic nephropathy causes destruction of the glomerulus, the structure responsible for the initial filtration of the blood. An early sign of this damage is the presence of protein in the urine, which typically starts in very small amounts in a condition known as microalbuminuria. As the kidney damage progresses, larger amounts of protein are detected in the urine in a condition known as proteinuria. Kidney failure results when waste products build up in the blood because the glomerulus has an impaired ability to filter and cleanse blood. People may lose two-thirds or more of their kidney function before symptoms appear; therefore, the American Diabetes Association recommends annual testing for the presence of protein or microalbumin. People who have type 2 diabetes account for most of the cases of diabetic kidney disease. Ways to prevent or slow kidney disease include controlling blood glucose levels, blood pressure, and cholesterol levels; considering using an angiotensin converting enzyme inhibitor; quitting tobacco use; and evaluating protein consumption. 1 figure.

- **Diabetes and Kidney Disease: The Importance of Proper Management and Prevention**

  Source: For Patients Only. 14(4): 22-24. July-August 2001.

  Contact: Available from For Patients Only. 18 East 41st Street, New York, NY 10017. (818) 704-5555. Fax (818) 704-6500.

  Summary: This article encourages readers with diabetes to take their disease seriously and to follow specific, ongoing measures to avoid the complication of kidney disease (diabetic nephropathy). Written for a newsletter for people with kidney disease, the article notes that at least four in 10 people with kidney disease can attribute their disease to diabetes. The author also cautions that kidney disease is just as likely to develop in individuals with type 2 diabetes as in those with type 1 diabetes. The author provides basic facts and statistics regarding diabetes and kidney disease and then focuses on the 'good news,' i.e., how to treat and perhaps even prevent diabetic nephropathy. The article includes a list of the symptoms of diabetes and the first signs of kidney disease in individuals with diabetes; a list of strategies that patients can follow to reduce their risk

of developing end stage renal disease (ESRD), and a brief discussion of the specific concerns in certain minority populations (such as American Indians and Alaskan Natives) who have higher rates of diabetes than white populations.

- **Fighting Diabetic Kidney Disease**

  Source: Diabetes Forecast. 55(2): 68-70. February 2002.

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

  Summary: This article helps readers with diabetes understand the strategies that can use to prevent or slow the kidney disease often associated with diabetes (diabetic nephropathy). The author reviews risk factors, how diabetes can have a negative impact on the kidneys, and the role of maintaining tight blood glucose control and controlling blood pressure. The author also offers suggestions for reducing the risks of diabetic nephropathy: treat urinary tract infections (UTIs) quickly and fully; avoid harmful medications; avoid x ray dyes whenever possible; and treat neurogenic bladder. The article concludes with guidelines for screening tests for diabetic nephropathy; the American Diabetes Association recommends yearly tests for urine protein (proteinuria).

- **Living with Kidney Disease**

  Source: Diabetes Self-Management. 15(6): 21, 25-26, 28, 30-31. November-December 1998.

  Contact: Available from R.A. Rapaport Publishing, Inc. 150 West 22nd Street, New York, NY 10011. (800) 234-0923.

  Summary: This article provides information on the progression, prevention, and treatment of diabetic nephropathy, which progressively damages the ability of the kidneys to perform their functions and may lead to a life-threatening condition called end-stage renal disease (ESRD). In People who have diabetes, the stages that occur in the progression to ESRD are hyperfiltration, microalbuminuria, overt diabetic nephropathy, advanced clinical nephropathy, and ESRD. The article presents ways to prevent diabetic nephropathy or to slow its progression, including maintaining tight blood sugar control, detecting signs of kidney disease early, normalizing blood pressure, using angiotensin-converting enzyme inhibitors, and eating a low-protein diet. The article discusses treatment options for ESRD, including hemodialysis, peritoneal dialysis, and kidney transplantation and highlights the advantages and disadvantages of each option. In addition, the article offers strategies for coping with ESRD, including acknowledging the grief and loss of a failed organ, finding a support network, and giving back to others. A list of support organizations is also included. 1 figure.

- **Prevention, Early Detection, and Aggressive Management of Diabetic Kidney Disease**

  Source: Clinical Diabetes. 16(2): 77-80. March-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 provides practical pointers for the prevention, early detection, and aggressive management of diabetic kidney disease (diabetic nephropathy). The author notes that diabetic nephropathy is responsible for a large amount of morbidity and mortality as well as approximately $1.5 billion per year in costs related to dialysis and kidney transplantation. The article describes the 5 stages of diabetic kidney disease;

later stages include incipient diabetic nephropathy, overt nephropathy, and end-stage renal disease. Proven therapeutic interventions to prevent or retard the progression of diabetic kidney disease include glucose control, blood pressure control, use of angiotensin-converting enzyme (ACE) inhibitors, and protein restriction. Cholesterol reduction and antioxidant therapy are two additional strategies that have not yet been well proven. The author concludes that the most powerful and proven method of prevention is to maintain strict glycemic control from the time of diabetes diagnosis. Annual microalbuminuria testing is currently the most sensitive technique for detecting early renal damage. The article concludes with a list of six suggested readings. 3 tables.

- **Researchers Plot to Prevent Diabetic Kidney Disease**

  Source: JDF International Countdown. 20(4): 14-18. Fall 1999.

  Contact: Available from Juvenile Diabetes Foundation International. 120 Wall Street, New York, NY 10005-4001. (800) 533-2873 or (212) 785-9500. Website: www.jdfcure.com.

  Summary: This article reviews research on diabetic nephropathy. The article begins with a discussion of the progression of diabetic nephropathy. This is followed by an examination of the role of hyperglycemia in the initiation and progression of diabetic nephropathy. Researchers agree that hyperglycemia is a crucial factor in the development of diabetic nephropathy. The smooth muscle cells found in the small blood vessel walls of the kidney do not rely on insulin for glucose intake, so they are directly exposed and vulnerable to high levels of glucose when blood sugar levels are high. If untreated, the gradual thickening and scarring of the glomeruli completely destroy its filtration capacity, and the kidneys stop working. Although the association between high blood sugar levels and kidney damage is conclusive, scientists must determine the precise sequence of molecular events that leads to the initial cellular alterations in the vessel walls of the kidneys before effective methods for early intervention and prevention can be developed. Theories for preventing diabetic nephropathy focus on the inhibition of advanced glycation end products and the inhibition of one or more of events triggering protein kinase C activation. In addition, the article highlights an international research project that is allowing researchers to study diabetic nephropathy in its earliest stages in human patients. In another study designed to identify early indicators of diabetic kidney disease, a researcher is investigating changes in the breakdown of albumin. Other topics addressed in the article include the relationship between high blood pressure and kidney disease, the role of genetics in the development of kidney disease, and the treatment of nephropathy with angiotensin converting enzyme inhibitors and calcium channel blockers. 2 figures.

- **Resistance Training Enhances the Value of Protein Restriction in the Treatment of Chronic Kidney Disease**

  Source: Annals of Internal Medicine. 135(11): 999-1001. December 4, 2001.

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

  Summary: This editorial considers data that demonstrates that resistance training enhances the value of protein restriction in the treatment of chronic kidney disease. Use of a low protein diet to slow progression of kidney disease is controversial, but is probably efficacious, even in patients with nephrotic range proteinuria (protein in the urine). The use of low protein diets in patients with renal insufficiency is usually not instituted without some concern for safety. Loss of lean body mass is common in

patients with chronic kidney disease. In the same issue as this editorial, a research article reports results that show that resistance exercise training can preserve lean body mass, nutritional status, and muscle function in patients with moderate chronic kidney disease who are consuming a low protein diet to slow the progression of renal (kidney) failure. The study's results suggest that resistance training is a safe and effective countermeasure to the negative effects of protein restriction on muscle mass accretion, protein utilization, nutritional status, and muscle function in patients with chronic kidney disease. The editorial author reiterates the importance of teaching kidney disease patients about the crucial role of exercise as part of a standard treatment regimen. 20 references.

Federally Funded Research on Kidney Disease

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

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

- **Project Title: AASK COHORT CLINICAL CENTER**

  Principal Investigator & Institution: Lea, Janice P.; Medicine; Emory University 1784 North Decatur Road Atlanta, Ga 30322

  Timing: Fiscal Year 2003; Project Start 30-SEP-1992; Project End 30-JUN-2004

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects on kidney function of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. For our clinical center, a total of 39 patients who have not reached dialysis will be enrolled, and a total of 9 patients who

[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).

have reached dialysis will be enrolled to obtain DNA only. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of reno-protective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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

- **Project Title: AASK COHORT STUDY**

  Principal Investigator & Institution: Phillips, Robert A.; Director, Department of Medicine; Lenox Hill Hospital 100 E 77Th St New York, Ny 10021

  Timing: Fiscal Year 2003; Project Start 19-AUG-1994; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication treatment for hypertension, beginning with angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of reno-protective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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

- **Project Title: AASK COHORT STUDY, CLINICAL CENTER #0-UCSD**

  Principal Investigator & Institution: Gabbai, Francis B.; Professor; Veterans Medical Research Fdn/San Diego Foundation of San Diego San Diego, Ca 92161

  Timing: Fiscal Year 2003; Project Start 15-AUG-1996; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and

Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of reno-protective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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

- **Project Title: AASK COHORT STUDY, CLINICAL RESEARCH CENTER AT MEHARRY**

  Principal Investigator & Institution: Faulkner, Marquetta L.; Associate Professor; Internal Medicine; Meharry Medical College 1005-D B Todd Blvd Nashville, Tn 37208

  Timing: Fiscal Year 2003; Project Start 29-SEP-2003; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects on kidney function of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of reno-protective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the

progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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

- **Project Title: AASK COLHORT STUDY**

  Principal Investigator & Institution: Wright, Jackson T.; Professor of Medicine; Medicine; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

  Timing: Fiscal Year 2003; Project Start 01-OCT-1995; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects on kidney function of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of reno-protective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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

- **Project Title: AASK NIH COHORT STUDY**

  Principal Investigator & Institution: Kopple, Joel D.; Professor; Harbor-Ucla Research & Educ Inst 1124 W Carson St Torrance, Ca 90502

  Timing: Fiscal Year 2003; Project Start 29-SEP-2003; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic,

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

- **Project Title: AASK: THE COHORT STUDY**

  Principal Investigator & Institution: Tisher, Charles C.; Professor of Medicine; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2003; Project Start 15-AUG-1994; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Approximately 48 of this Center's AASK participants who have not yet reached end stage disease will be enrolled into the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of reno-protective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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

- **Project Title: ADPKD:DISEASE SPECTRUM & GENOTYPE-PHENOTYPE CORRELATIONS**

  Principal Investigator & Institution: Harris, Peter C.; Professor of Medicine; Mayo Clinic Rochester 200 1St St Sw Rochester, Mn 55905

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

  Summary: (provided by applicant): Molecular diagnosis of autosomal dominant polycystic **kidney disease** (ADPKD) has proven difficult because of genetic and allelic heterogeneity and the complex structure of the major gene, PKD1. Consequently, the

degree to which the marked phenotypic variability in the severity of renal disease and expression of extrarenal manifestations correlates with genotype is largely unknown. Using recent improvements to specifically amplify the PKDI gene and temperature modulated heteroduplex analysis (TMHA), we propose to develop rapid and accurate genetic characterization of the ADPKD genes. Mutation detection rates of >80 percent for PKD1 and >90 percent for PKD2 will be achieved during the project. The fate and stability of mutant ADPKD proteins, polycystin-1 and -2, will be investigated in patient-derived lymphoblastoid cell lines, epithelial cell lines derived from a single cyst lining, and knockout mouse models of PkdI. The mutational mechanism will be further explored by the isolation of individual cyst lining, characterized by their immuno-reactivity to the polycystin proteins, using laser capture microdissection. Genetic analysis of these cells will reveal the importance of somatic events at the ADPKD genes and elsewhere for cyst initiation and expansion. Phenotype/genotype correlations will be explored in defined patient groups: renal insufficient; geographically defined without referral or recognition bias; very early onset disease; late onset disease; severe liver disease and vascular abnormalities. The ADPKD gene is known to be a strong indicator of renal disease severity (PKD1 more severe than PKD2) but the relative contribution of the two genes to extra-renal disease is unknown. The prevalence of PKD2 in the general population is also largely unknown. Correlations between the type and position of mutation in PKD1 and PKD2 will be made to the severity of renal disease and to the different phenotypic groups. These results will show if there are clear phenotype/genotype correlations, that may have prognostic implications, reveal more about the mutational mechanism and highlight important regions of the polycystin proteins. Specific mutational mechanisms, such as an early embryonic somatic mutation or the modifying effect of variants at the ADPKD allele inherited from the normal parent, will be analyzed in early onset cases. This study will help resolve questions about the mutational mechanism in ADPKD, determine the role of somatic events, show the extent to which the ADPKD genotype dictates clinical outcomes and generate phenotypically and genotypically well characterized ADPKD populations that will be suitable for testing the role of other genetic modifying factors.

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- **Project Title: AFRICAN AMERICAN STUDY OF KIDNEY DISEASE & HYPERTENSION**

  Principal Investigator & Institution: Pogue, Velvie A.; Medicine; Columbia University Health Sciences New York, Ny 10032

  Timing: Fiscal Year 2003; Project Start 29-SEP-2003; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects on kidney function of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal

outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of renoprotective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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

- **Project Title: AFRICAN AMERICAN STUDY OF KIDNEY DISEASE & HYPERTENSION**

  Principal Investigator & Institution: Randall, Otelio S.; Professor of Medicine; Medicine; Howard University 2400 6Th St Nw Washington, Dc 20059

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

  Summary: Hypertension is considered one of the major causes of end stage renal disease (ESRD) in the general population, and the number one cause in African Americans. Despite the availability of potent antihypertensive drugs, the number of hypertensive African Americans progressing to ESRD continues to rise. This disproportionately high prevalence of ESRD in African Americans cannot be explained by the higher prevalence of hypertension. Whether this is due to more susceptibility of the kidney of African Americans to hypertensive injury or due to concurrent existence of unidentified renal factors is not known. There is preliminary evidence suggesting that antihypertensive drugs may retard the progression of hypertensive renal disease, but no clinical trial has been conducted to test this hypothesis in African Americans. This proposed multi-center project is designed to study the following: if the pathological lesion in "hypertensive renal disease" is purely a result of persistent hypertension; if one anti-hypertensive drug is better than another in terms of preservation of renal function; and the level of blood pressure suitable for the survival of the kidney. Hypertensive African Americans, 18-70 years of age with no other known disease that can affect the kidney, will be screened for blood pressure qualification, and will undergo glomerular filtration rate (GFR) tests. Those who qualify, based on blood pressure levels and the GFR results will then be randomized in a double-masked fashion to one of the three major antihypertensive classes (converting enzyme inhibitor, calcium channel blocker, or beta blocker) and to one of two pressure levels: mean blood pressure greater than 92 millimeter of mercury (mmHg), or 102 to 107 mmHg. Other antihypertensive drugs will be added to keep the blood pressure at the desired level. The blood pressure of the randomized subjects will then be monitored on a monthly basis and compliance to medication(s) will be checked at the same time. Their renal function will also be tracked with periodic GFR tests throughout the study period, which will last approximately four years. All data will be collected and sent to the Data Coordinating Center (DCC) for analyses and interpretation. The goal of the African American Study of **Kidney Disease** and Hypertension (AASK) full- scale trial is to better understand the physiopathology of hypertensive renal disease in an effort to develop guidelines to prevent the increasing prevalence of ESRD in African Americans.

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

- **Project Title: AFRICAN AMERICAN STUDY OF KIDNEY DISEASE AND HYPERTENSI***

  Principal Investigator & Institution: Toto, Robert D.; Professor of Internal Medicine; Internal Medicine; University of Texas Sw Med Ctr/Dallas Dallas, Tx 753909105

  Timing: Fiscal Year 2003; Project Start 30-SEP-1992; Project End 30-JUN-2004

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects on kidney function of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socioeconomic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of renoprotective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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

- **Project Title: AFRICAN-AMERICAN STUDY OF KIDNEY DISEASE /HYPERTENSION**

  Principal Investigator & Institution: Rostand, Stephen G.; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2003; Project Start 19-AUG-1994; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended anti-hypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects on kidney function of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD,

or death. Medication treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of reno-protective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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

- **Project Title: AGE SIGNALING IN DIABETIC RENAL DISEASE**

  Principal Investigator & Institution: Xu, Dazhong; New England Medical Center Hospitals 750 Washington St Boston, Ma 021111533

  Timing: Fiscal Year 2002; Project Start 01-JUL-2002; Project End 30-JUN-2005

  Summary: (provided by applicant): Nephropathy is one of the major complications of both type 1 and type 2 diabetes mellitus. Thus approximately 40% of individuals with diabetes will develop **kidney disease,** and renal failure accounts for a significant proportion of the mortality attributable to diabetes. The progression to diabetic **kidney disease** is a complex and poorly understood process. Elevated plasma glucose triggers the secretion of transforming growth factor-beta (TGF-Beta) which, in turn, stimulates the pathologically excessive deposition of extracellular matrix-a process mediated by glomerular mesangial cells. Elevated blood glucose also stimulates mesangial cell hyperplasia and hypertrophy. These processes eventually culminate in renal failure. While a direct signaling role for glucose has been proposed, glucose itself is a weak mesangial cell agonist. Advanced glycation endproducts (AGEs), formed by the nonenzymatic glycation of proteins and lipids, are present in excess in diabetes and are thought to be important early in the development of diabetic renal disease. AGEs exert their effects by interacting with the receptor for advanced glycation endproducts (RAGE). RAGE expression is elevated in diabetes. Blockade of RAGE has been shown to suppress vascular hyperpermeabiity and accelerated atherosclerosis in diabetic rats. These results, suggest that AGEs/RAGE play a central role in triggering the early pathophysiologic changes associated with diabetic nephropathy. Accordingly, investigating RAGE intracellular signaling mechanisms and cellular effects is important to furthering our understanding of diabetic renal disease. We propose two broad areas of study: dissection of the signaling pathways coupling mesangial cell RAGE to ERK and PI-3-kinase and identification of signaling elements recruited by RAGE that are important to pathophysiologic changes of mesangial cells associated with diabetes.

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

- **Project Title: AGE-RECEPTORS AND KIDNEY DISEASE**

  Principal Investigator & Institution: Vlassara, Helen; Professor; Medicine; Mount Sinai School of Medicine of Nyu of New York University New York, Ny 10029

  Timing: Fiscal Year 2001; Project Start 01-AUG-2000; Project End 31-JUL-2004

  Summary: Substantial evidence suggests that genetic factors predispose patients to diabetic renal disease, which can be exacerbated by poorly managed hyperglycemia. Glucose-derived Advanced Glycation Endproducts (AGE) that accumulate with aging and, at an accelerated rate in vascular and renal tissues in both IDDM and NIDDM subjects have been linked to irreversible renal damage. Recent human studies have

revealed a major environmental risk factor that can exacerbate renal disease in DM: dietary AGEs (glycotoxins) that are abundant in foods. A cell-associated AGE-specific receptor (AGE-R) system, present on numerous cells and several glomerular components, including mesangial cells (MC) and endothelium, modulates growth-related mediators and matrix synthesis in vitro. Thus, AGE-R interactions with native and environmental AGEs in vivo may be instrumental in diabetes- and age-related nephropathy. In susceptible individuals, the AGE-receptor expression/function is subject to environment- and/or gene-related alterations, which, together with metabolic/hormonal factors of diabetes, may influence renal cell and matrix gene functions. Preliminary data suggest altered level, and activity of AGE-R in MC from non-obese diabetic (NOD) mice as well as in blood cells of DN-prone IDDM patients. The goals of this proposal are to explore: 1) the in vitro regulation of the glomerulus-specific MC AGE-R by modulators associated with diabetes: glucose, insulin, AGEs, growth factors/cytokines; 2a) to establish the in vivo dysregulation of the glomerular AGE-R expression/function by diabetes, using diabetes-prone animal models susceptible (NOD) or resistant (BB/Wor) to DN, and AGE-infused, non-diabetic animals, 2b) to elucidate in vivo turnover of dietary-AGE and its contribution to AGE-R dysfunction in DN susceptible animals, 3a) to explore the relationship of human DN with the level of expression of AGE-R activity in blood mononuclear cells (PBM) and EBV-transformed lymphoblast cell lines from DM patients wit/without DN, and 3B) to begin exploring whether AGE-R gene mutations/defects contribute to the susceptibility of certain persons to DN. The findings are intended to: provide insights for new therapeutic targets and/or novel methods for early detection of, and intervention with diabetic **kidney disease.** Since aging-related nephropathy shares significant aspects of AGE toxicity, as well as of diabetes and its complications, the positive outcome of these studies is likely to benefit both rapidly expanding populations, diabetic and nondiabetic adults.

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

- **Project Title: ALTERED EXOCYTOSIS AND RABS IN POLYCYSTIC KIDNEY DISEASE**

  Principal Investigator & Institution: Wandinger-Ness, Angela U.; Associate Professor; Pathology; University of New Mexico Albuquerque Controller's Office Albuquerque, Nm 87131

  Timing: Fiscal Year 2001; Project Start 15-AUG-1995; Project End 31-JUL-2001

  Summary: Autosomal dominant polycystic **kidney disease** (ADPKD) is a leading cause of renal failure for which there is no known treatment. The causal gene in 85% of all cases has recently been cloned, however the function of its protein product as well as the mechanisms whereby mutations in this gene lead to the pathogenesis of the disease remain a mystery. It is the aim of this proposal to combine cellular and biochemical approaches to further our understanding of the primary cause(s) of ADPKD. Numerous cellular functions have been reported to be affected in this disease, however, many of these might be explained by an alteration in the renal epithelial cell program specifying polarized membrane transport. This is a testable hypothesis which will be examined by measuring both protein and lipid sorting in primary normal or polycystic human kidney cells. The approaches will quantify any alterations in the transport kinetics as well as in the polarized delivery of these molecules. Thus, simple assays for measuring phenotypic alterations specifically associated with ADPKD and crucial for the evaluation of the disease gene function will be developed. In parallel, the protein compositions of normal and polycystic kidney cells will be compared by two-dimensional gel electrophoresis

with the initial aim of establishing whether molecules known to be involved in membrane transport as well as those encoded by the PKD1 locus are affected in order to pinpoint the primary effectors. In the long-run, determining the extent of the changes in protein expression patterns manifested in ADPKD and using this as a functional assay for evaluating how genes at the PKD1 locus might influence these changes is expected to provide important clues concerning the mechanisms underlying the pathogenesis of the disease. The PKD1 locus contains as many as 20 genes, which are thought to be part of a genomic cluster of genes with important regulatory functions in kidney epithelial cell differentiation. Two of these genes are of particular interest because of their functions and their immediate proximity to the disease gene, PBP. One is the TSC2 gene which when mutated also causes renal disease and the second is the NIK7 gene which specifies a novel rab GTPase, not previously identified. The rab GTPases are known to be important regulators of intracellular membrane transport since dominant negative mutations have a drastic inhibitory effect on these processes. Thus far only one rab GTPase has been clearly demonstrated to be specifically expressed in epithelial cells and two others are currently under investigation. These facts suggest that the analysis of these two neighboring genes may shed some light on kidney epithelial development and/or on the disease process. Experiments will compare the expression of TSC2 and NIK7 in normal and polycystic kidney and investigate the subcellular localization of these proteins to reveal their possible functions. Coupled with the assays for quantifying ADPKD specific phenotypic changes it will be possible to evaluate directly the role of these genes in the disease process. In summary, the long-term goals of this work are to identify important regulators of specialized epithelial cell functions and to understand how these are subverted to give rise to ADPKD.

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

- **Project Title: BIOLOGY OF EARLY RENAL CYSTOGENESIS IN THE CPK MOUSE**

  Principal Investigator & Institution: Guay-Woodford, Lisa M.; Pediatric Nephrologist; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

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

  Summary: (Adapted from the investigator's Abstract): Emerging evidence indicates that renal cystic disease in both humans and mouse models involves a multigenic pathway in which the disease-susceptibility genes act by cellular recessive mechanisms. These genes also appear to play critical roles in renal differentiation and maturation. The cpk mouse was the first polycystic **kidney disease** (PKD) model to be described and as such, it has been the most extensively characterized. While these studies have significantly contributed to our understanding of renal cystic disease, they have been conducted primarily in mice with advanced renal cystic disease. Therefore, the critical relationship between the normal epithelial differentiation and the initial events of renal cyst formation remains to be elucidated and the molecular basis for the cpk phenotype is as yet unknown. The ultimate goals of the PI are (1) to characterize the role of the cpk gene product in renal development by determining the molecular pathways in which it functions, and (2) to elucidate how the loss of function of this gene causes renal cyst formation. In this grant application, the PI proposes to establish the biologic and molecular framework for these investigations. The proposal is divided into two complementary projects. First, in Aim 1, they propose to test whether the prevailing hypotheses regarding renal cystogenesis apply to the genetically-defined, fetal cpk model that they have recently characterized. Second, they propose to clone the cpk gene. Aim 2 deals with the construction of a complete transcript map of the critical cpk interval. Aim 3 deals with the identification of the cpk gene from the transcript map

generated. In Aim 4 they propose to examine the temporal and spatial expression of the cpk gene during the stages of renal organogenesis, e.g. induction, acquisition of stem cell character, fate determination, condensation, epitheliogenesis, polarization, and maturation. Significance: The cpk mutation represents one of a number of recessive +_____ mutations causing PKD in the mouse. Like most other spontaneous mutations, the severe **kidney disease** of this mutant demonstrates the importance of the normal cpk counterpart in renal function. Given that the mechanism of cystogenesis is not well understood, despite the information provided by the cloning of PKD1 and PKD2. There is an increased need for discovering new genes in mouse whose deregulation leads to renal cystogenesis. The preliminary work from the laboratories of the principal investigator and the collaborators has resulted in the placement of the cpk mutation to a region between D12Mit218 and D12Mit105 of mouse Chr 12. Based on recombination frequency the two flanking markers were placed 0.26 cM apart (approximately 5 X 10 exp 5 bp). The physical map of the cpk critical region is being generated. Based on the fine mapping data the human cpk homologue maps to Chr 2p24-2p25. The physical map is being generated. Approach: Specific Aim 1: Examine the prevailing hypotheses regarding renal +_____ cystogenesis in fetal cpk mouse model. a) disruption in basement membrane 1 PATHOLOGY A SS 3 R01 DK55534-01A1 June, 1999 Guay-Woodford, Lisa M formation. b) dysregulation of cell proliferation and apoptosis. c) aberrant expression of the epidermal growth factor receptor (EGFR), polycystin, and polycystin-2. The hypothesis is that the loss of function of the cpk gene interrupts the terminal phases of renal tubulo-epithelial differentiation. They speculate that the proximate event in renal cystogenesis may be a dysregulation of basement membrane composition with subsequent dysregulation of cell-matrix interactions, cell proliferation, and apoptosis that occur in a hierarchical order. In order to test this they plan to examine the expression of entactin-1, laminin gamma1, polycystin-1, polycystin-2 and EGF-R in E15 control (+/+) and cpk/cpk kidneys. They also propose to analyze the cell proliferation and apoptosis in the same. The E15 kidney was chosen since light microscopy revealed tubular dilation only in pups homozygous for B6 alleles. This experiment will provide answers with respect to the altered events in the E15 diseased kidney due to the loss of the cpk gene. However, in order to either confirm or refute the hierarchical order speculated it may be important to study the developmental profile of all the factors proposed during cystogenic process (Time points earlier and later than E15 have to be considered). Specific Aim 2: Isolate all expressed sequences from the cpk candidate interval and construct a complete transcript map of the interval. Based on the Whitehead/MIT database a YAC contig that spanned the 0.26cM interval was generated. Presently they have almost generated a BAC contig of this region. Unfortunately the interval is rather large (750kb). The chance of cutting down this interval considerably is rather remote. Since, only two recombination events in this interval were noted previously and the supplemental data suggests that the SP6 end of BAC-358F10 does not cross the distal recombination event in BC65. In light of their latest results, the identification of additional polymorphic markers to further refine the recombination breakpoints of the cpk interval can take a backseat. The identification of all the expressed sequences from the cpk interval must take priority. As the PI has pointed out Exon trapping, Hybrid cDNA selection and EST database analysis are the ways to go. The use of shot-gun sequencing is not an economical approach especially with a region as big as 750kb (requiring 8,000-12,000 sequencing). Specific Aim 3: Analyze candidate transcripts and identify the cpk gene. The methods proposed by the investigator to analyze the coding part of the candidate genes isolated are logical and well thought out. However, no methods have been discussed to detect mutations in the promoter or intronic region. The in vitro functional complementation assay proposed to test the candidate cpk +__ _____ gene is not established at this juncture. Specific Aim 4:

Characterize the temporal and spatial expression of the cpk gene in the mouse fetal kidney. The experiments designed to analyze the expression of the cpk gene in mouse fetal kidney are described well. Innovation: The project does employ a number of new methods and approaches. +_____ 1 PATHOLOGY A SS 4 R01 DK55534-01A1 June, 1999 Guay-Woodford, Lisa M However the project does not challenge any existing paradigms or develop new methodologies. This does not however weaken the application. Investigator: Dr. Guay-Woodford appears to have the technical and intellectual +_____ skills to accomplish the cloning of the cpk gene. Environment: The environment at University of Alabama School of Medicine +_____ appears to be conducive for the research proposed by the investigator. OVERALL EVALUATION: This proposal represents important steps that have to be +_____ taken to further our understanding of the cpk locus. However the principal weakness of this proposal is Aim 1, the experiments designed do not answer the questions proposed by the PI. As already mentioned a more detailed experimental protocol is required to confirm or refute the speculations. Thus, it would be better to concentrate on the cloning of cpk gene.

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

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

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

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

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

be guided by a three- dimensional model of the pore, proposed in the application, which takes into account the experimental data for TM domains 5, 6, 11, and 12. This approach hypothesizes that multiple helical domains contribute both to the binding sites for drugs and to the determinants of selectivity in the channel. A specific subset of residues that may determine the biophysical features of permeation is proposed. Testing the importance of these residues will allow the construction of a detailed map of the conduction pathway. An improved understanding of the function of this channel will aid in the design of novel therapies for Cystic Fibrosis, secretory diarrhea, and polycystic **kidney disease.**

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

- **Project Title: CASPASES AND APOPTOSIS IN ADPKD**

  Principal Investigator & Institution: Edelstein, Charles L.; Associate Professor of Medicine; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

  Timing: Fiscal Year 2001; Project Start 01-APR-1985; Project End 30-JUN-2006

  Summary: Autosomal Dominant Polycystic **kidney Disease** (ADPKD) is the most common life threatening hereditary disease in the USA and it accounts for about 5-10% of end-stage renal failure requiring dialysis and renal transplantation. Apoptosis in cells lining the cysts as well as in non-cystic is a characteristic feature of animal models of ADPKD as well as human ADPKD. Apoptosis is thought to play a role in both cyst formation and the loss of normal tubules and subsequent renal failure. The central component of the apoptosis machinery is a novel family of cysteine proteases called caspases. Cell permeable caspase inhibitors have been widely used in animal studies in vivo to dramatically alter a variety of pathological processes. The effect of caspase inhibition on apoptosis, proliferation, cyst formation and renal failure in ADPKD forms the basis of this grant proposal. The overall hypothesis presented in this grant proposes that dysregulation of the balance between pro and anti-apoptotic Bcl-2 family proteins leads to activation of the "initiator" caspases 8 or 9 and the "executioner" caspase-3. Further, it is proposed that apoptosis precedes proliferation leading to cyst formation and that apoptotic loss of non-cystic renal tubules leads to renal failure. Complementary studies will be performed in Han:SPRD rats and Pkd2 mutant mice, which closely resemble human ADPKD. In Specific Aim #1 we shall describe the time course and localization of apoptosis and proliferation. Specific Aim #2 focuses on in vivo studies to determine whether caspase inhibitors will attenuate apoptosis, proliferation, cyst formation and renal failure. Caspase activity, protein and gene expression will be measured. Functional (serum urea and creatinine) and morphological (renal cyst size, proliferation and apoptosis) correlates will be documented. In Specific Aim #3, the relationship between Bcl-2 gene family protein expression and caspase-3 activity will determined. The potential relevance of these studies to clinical ADPKD is substantial and the results should provide leads to altering the course of ADPKD. This is particularly true because of the current availability of cell permeable, non toxic caspase antagonists that are active in vivo.

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

- **Project Title: CELL INTERACTIONS IN DEVELOPMENT OF THE MAMMALIAN KIDNEY**

  Principal Investigator & Institution: Mcmahon, Andrew P.; Professor; Molecular and Cellular Biology; Harvard University Holyoke Center 727 Cambridge, Ma 02138

Timing: Fiscal Year 2001; Project Start 01-SEP-1998; Project End 31-AUG-2003

Summary: A vital part of understanding the pathology of organ systems in the human body is to determine the developmental mechanisms responsible for their induction, patterning, growth and differentiation. Alterations in any one of these processes can lead to debilitating or life- threatening diseases. One example is polycystic **kidney disease** (PKD) which accounts for 8 percent of all cases of end state renal **kidney disease.** PKD is thought to result from a failure in differentiation of nephronic epithelia, underscoring the need to study mechanisms operating in embryonic life to understand adult disease. The long term goal is elucidation of how the nephron, the excretory unit of the kidney, is formed. The studies focus on the roles of two families of signals, Wnts and Hedgehogs whose role is patterning the early embryo of diverse animal species is well substantiated. The hypothesis is that these same signals are recruited later in development to regulate organ development. To test this hypothesis, the Principal Investigator has chosen the kidney as a model. The choice reflects the rich embryological history associated with this organ, the excellent culture systems available to study interactions and the relevance to human disease. Nephron formation requires inductive signaling between a branching tubular epithelial network, the ureteric bud, and adjacent mesenchymal cells. The ureteric bud induces formation of simple, epithelial tubules. These, then undergo a complex morphogenesis, fusing with the ureteric bud-derived collecting duct system, to generate the tubular network of the nephron. Wnt-4 is a mesenchymal signal required for tubule induction. The Principal Investigator will use culture of kidney rudiments and analysis of mouse mutants to determine whether Wnt-4's action is antagonized by a binding partner, sFRP2. Growth of the ureteric epithelium is dependent on cRET activation at the tips. The Principal Investigator will use genetic approaches to investigate the potential role of two Wnts, Wnt-11 and Wnt-6, in this process. Further, the Principal Investigator will use transgenic mice to investigate whether local activation of cRET is required for branching. To determine whether microtubule based processes are involved in branching they will generate transgenic strains to visualize microtubules in the ureteric bud. More distal regions of the ureteric epithelium do not branch, and express distinct signals, Wnt-7b and Shh. Their roles in this region of the kidney will be determined by genetically modifying their expression. These approaches will include the development of new transgenic mouse strains which will allow both tissue and temporal regulation of gene expression in the ureteric bud and its derivatives. Finally, given the importance of Wnt-signals, they will start to examine their receptors in the kidney.

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

- **Project Title: CELLULAR MECHANISM OF DIABETIC NEPHROPATHY**

  Principal Investigator & Institution: Feng, Lili; Professor; Medicine; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

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

  Summary: The objective of this proposal is the understanding of cellular mechanisms associated with the progression of diabetic nephropathy. Diabetic nephropathy is the single largest cause of end-stage renal failure in the United States. The disease is believed to be triggered by hyperglycemia in diabetes mellitus, Previous studies by others and us have show that increased expression of cytokines and growth factors play an important role in the development of **kidney disease.** The mitogen- activated protein kinase (MAP kinase) family members are involved in the activation of cytokines and growth factors in renal cells exposed to high glucose, but also participate in the subsequent signal transduction of these cytokines and growth factors to mediate further

cellular changes. Inhibition of a MAP kinase family member, p38, by a selective inhibitor dramatically suppressed the progression of diabetic nephropathy in a rat model (streptozotocin-induced diabetes), and activation of p38 significantly accelerated the development of diabetic nephropathy. In this application, we propose to carry out studies designed to determine the function of each MAP kinase family member in diabetic nephropathy. Specifically, we will address the role of these MAP kinases in high glucose-induced gene expression and in growth factor- and cytokine- induced renal cell activation, utilizing biochemical, molecular biological, and immunological approaches. In vivo experiments will be performed to confirm the results obtained in the in vitro studies and to develop a better understanding to the role of MAP kinases in various stages of the pathogenesis of diabetic nephropathy. Insights gained in the proposed studies will lead to the development of new therapeutic strategies to this life-threatening disease.

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

- **Project Title: CHEMOKINE THERAPEUTIC TARGETS FOR KIDNEY DISEASE**

  Principal Investigator & Institution: Kelley, Vicki R.; Associate Professor; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

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

  Summary: n influx of leukocytes is common to progressive kidney diseases. Targeting specific molecules responsible for recruitment of leukocytes into the kidney provides a therapeutic strategy for halting tissue progressive damage. Monocyte chemoattractant protein-1(MCP-1) belongs to a family of "chemokines" which attract leukocytes to tissues targeted for inflammation. MCP-l is abundantly expressed by renal parenchymal cells during progressive renal injury. Blockade of MCP-l reduces the influx of activated macrophages, thereby sparing the tubules from macrophage mediated apoptotic destruction in acute nephrotoxic serum nephritis. The MRL-Faslpr model is appealing to identify therapeutic targets for progressive **kidney disease** since renal destruction is spontaneous, steadily progressive, predictable, fatal and shares features with human illnesses. **Kidney disease** in the MRL-Faslpr model is complex and consists of glomerular, tubular and peri-vascular damage, accompanied by an robust influx of macrophages and lymphocytes. MCP-1 is vigorously expressed in the MRL-Faslpr kidney prior to injury, and increases with advancing disease. We have constructed an MRL-Faslpr strain genetically deficient in MCP-1 and determined that mice lacking MCP-l live far longer than the wild-type strain. Using genetic approaches, we propose to test the hypothesis that MCP-1 is a therapeutic target for progressive autoimmune **kidney disease.** We propose to: 1) determine whether MCP-1 is required for autoimmune renal disease. We will establish whether MCP-1(-/-) deficient MRL-Faslpr mice are protected from **kidney disease,** and determine whether protection is exclusive to the kidney, or is systemic. 2) determine whether delivery of MCP-1 into the kidney amplifies or incites progressive renal disease. Using a retroviral gene transfer approach that provides for sustained delivery of MCP-l to a discrete area of the kidney, we propose to determine the impact of local MCP-1 expression on renal pathology, and to investigate whether MCP-1 restores pathology within a discrete area in MCP-l deficient MRL-Faslpr kidneys. We will establish whether MCP-1 is required for autoimmune nephritis in the NZM241O strain. 3) establish whether delivery of MCP-1 receptor antagonist (MCP-1ra) into the MRLFaslpr kidney prevents injury. We propose to: deliver MCP-lra to a discrete segment of the kidney using an ex vivo retroviral gene transfer and throughout the kidney using a lentiviral vector in vivo. We will establish the crucial period for MCP- 1 r blockade via a tetracycline transactivator system to

switch delivery of MCP- ira "on and off" at stages during the progression of nephritis. 4) establish the role of chemokines that share the CCR2 with MCP-1 in MRL-Faslpr mice. We propose to compare renal disease in MRL-Faslprstrains deficient in CCR2 and MCP-l to establish whether other MCPs are potential_therapeutic targets for **kidney disease.**

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- **Project Title: CHRONIC KIDNEY DISEASE IN CHILDREN STUDY (C-KID)**

  Principal Investigator & Institution: Furth, Susan L.; Pediatrics; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

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

  Summary: (provided by applicant): Chronic **kidney disease** (CKD) and its metabolic derangements substantially affect the well-being of children. In order to define the nature, magnitude, and temporal evolution of the adverse effects of progressive CKD, we propose to conduct a prospective study of CKD in children to determine (1) risk factors for accelerated decline in renal function; (2) incidence, nature, magnitude and temporal evolution of impaired brain function and structure; (3) prevalence of risk factors for cardiovascular disease (CVD); and (4) implications of growth failure and its treatment on morbidity. The Prospective Study of Chronic **Kidney Disease** in Children (C-Kid) is a longitudinal, observational study of 600 children, aged < 19 yrs with mildly to moderately impaired kidney function (estimated glomerular filtration rate (GFR) 30-75 ml/min/1.73m2). The follow-up period will be 2.5 to 4.5 years. At enrollment, and at annual visits thereafter, selected exposures will be obtained on participants, including sociodemographic characteristics, family history, health care utilization, environmental exposures and medication use using standardized questionnaires. Standardized blood pressure, growth and nutritional assessments, metabolic status, measures of anemia, dyslipidemia, measures of microinflammation, insulin resistance and proteinuria will also be measured. Level of kidney function (GFR) will be measured annually by plasma disappearance of iohexol. The primary outcomes of interest will be the temporal evolution of subclinical measures and clinical events associated with CKD progression as measured by decline in GFR, growth failure and its treatment, neurocognitive and behavioral deficits and cardiovascular disease, specified in our aims below. Potential analyses that could be conducted using the C-Kid infrastructure to explore risk-factor disease relationships include traditional prospective cohort analyses where putative risk factors are measured in participants at baseline; nested case-control studies in which laboratory studies are performed on stored baseline specimens in cases (e.g. rapid progressors) and appropriately matched controls (e.g. non-progressors); and cross-cohort analyses utilizing parallel cohorts.

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

- **Project Title: CLINICAL TRANSLATIONAL RESEARCH IN TRANSPLANT NEPHROLOGY**

  Principal Investigator & Institution: Becker, Bryan N.; Assistant Professor of Medicine; Medicine; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2002; Project Start 15-AUG-2002; Project End 31-JUL-2007

  Summary: (provided by applicant): There is grave concern that patient-oriented research is failing as a result of many factors now affecting the healthcare climate in academic settings, including a lack of mentoring and nurturing on the part of more established investigators. This problem is felt even more acutely in Nephrology, even as the clinical demand for Nephrologists is increasing to accomodate the workload of **kidney disease**

in the United States. The major goals of this project are to develop a program that fosters interest, curiosity and productivity among young investigators interested in patient-oriented research and Nephrology and gain insights that may lead to better outcomes for patients with **kidney disease.** The research program compiled by the Principal Investigator (P.I.) combines outstanding aspects of the University of Wisconsin-Madison (UW) environment with the excellence of the UW transplant program to develop clinical translational research in transplantation as the steppingstone for a larger and more complete Nephrology patient-oriented research program in the future. The P.I. has assembled resources to 1) expand training and mentoring opportunities in the UW Nephrology Section through patient-oriented clinical translational and mechanistic studies; and 2) allow him to mentor a new generation of Nephrologists interested in patient-oriented research. The research plan investigates mechanisms of allograft function and novel immunotherapeutics. The natural outgrowth of this work will be the expansion of patient-oriented research endeavors into areas of novel diagnostics and interventions for **kidney disease,** as well as quality-of-care and cost-effectiveness analyses encompassed within kidney disease-related outcomes research. The mentoring program is targeted at post-doctoral fellows and junior faculty. It is comprised of a) a learning plan; b) core curricula in patient-oriented research; c) specialized classes related to research activities; and d) direct involvement in mentored patient-oriented research projects. Many aspects of this work will be coordinated through the UW's Clinical Investigator Preparatory Program (CIPP). This grant will not only help yield new information about aspects of kidney function that hopefully will have a beneficial impact on clinical outcomes. It will also work to meet the NIH's goal of increasing the number of physician-scientists conducting high-quality patient-oriented research.

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- **Project Title: COLLECTING DUCT & ASCENDING LIMB-SPECIFIC GENE TARGETING**

  Principal Investigator & Institution: Kohan, Donald E.; Chief, Division of Nephrology; Internal Medicine; University of Utah 200 S University St Salt Lake City, Ut 84112

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-AUG-2003

  Summary: This proposal involves the development of transgenic mice expressing Cre recombinase targeted to the renal collecting duct and the thick ascending limb of Henle's loop. These two nephron segments are of fundamental importance in the regulation of renal electrolyte and water transport and are relevant to human diseases including congestive heart failure, cirrhosis, nephrotic syndrome, hypertension, renal stone formation, urine concentrating and diluting disorders and other kidney diseases. The collecting duct and thick ascending limb are also involved in a variety of developmental disorders, including polycystic **kidney disease** and medullary sponge kidney. Targeted Cre recombinase transgenic mice will facilitate the development of mice containing cell-specific genetic disruptions of genes thought to be involved in renal development, function or disease conditions. Limiting disruption of candidate genes to specific renal cell types may overcome problems associated with conventional targeting techniques which disrupt genes in all cells of the body that often result in abnormal and even lethal phenotypes. In this research proposal, transgenic mice containing an aquaporin-2 or a uromodulin promoter driving the expression of Cre recombinase will be developed to produce active Cre recombinase in the renal collecting duct and thick ascending limb of Henle's loop, respectively. Multiple founders for each cell type specific target will be developed to assure lines of mice with adequate cell specificity and Cre expression. These animals will be extensively characterized with regard to their ability to cause

collecting duct or thick ascending limb-specific gene disruption. Ultimately, the mice will be highly useful in studies directed at evaluating the role of gene products in renal development, function and disease.

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- **Project Title: CONFERENCE ON AUTOIMMUNITY & TOLERANCE IN RENAL DISEASE**

  Principal Investigator & Institution: Platt, Jeffrey L.; Director; Mayo Clinic Rochester 200 1St St Sw Rochester, Mn 55905

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

  Summary: (provided by applicant): The proposed conference would be co-sponsored by the National Institutes of Health and the American Society of Nephrology. The conference program is being developed by the Basic Science Committee of the American Society of Nephrology. Recent advances in immunology have shed light on basic mechanisms underlying autoimmunity, tolerance, and on the means by which autoimmunity injures organs such as the kidney. While these advances have been considerable, only limited progresss has been made in connecting fundamental observations with the pathogenesis of glomerular and interstitial disease of the kidney. This conference will bring together scientists engaged in the study of basic immunology with investigators studying the manifestations of end-organ injury. Among the subjects to be taken up at the conference are new insights into the activation and function of T and B lymphocytes, the means by which the products of T and B lymphocytes contribute to tissue injury, and the control of lymphocyte function in autoimmune disease. New information regarding effector functions of antibodies and complement and control of complement will be presented. Focus will also be directed at how organs and tissues respond to immune challenge. Also to be considered, is how basic mechanisms can be exploited for therapeutic purposes. The synthesis emerging from this conference gives rise to new ideas, collaborations and approaches to dealing with autoimmunity and tolerance in the context of **kidney disease.** Topics to be discussed: * New insights into the activation and function of T and B lymphocytes; * Means by which the products of T and B lymphocytes contribute to tissue injury; * Control of lymphocyte function in autoimmune disease; * New information regarding effector functions of antibodies; * Complement and control of complement; * How basic mechanisms can be exploited for therapeutic purpose.

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

- **Project Title: CORE--RENAL-KIDNEY DISEASE RESEARCH**

  Principal Investigator & Institution: Fink, Jeffrey C.; University of Maryland Balt Prof School Baltimore, Md 21201

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

  Summary: The aims of the Renal Research Core are: Specific Aim 1: Merge the complementary elements of the UMSHN and ERI program at UMB to enhance the primary missions of each entity and develop a unified action plan within the **Kidney Disease** Research Core. Specific Aim 2: Utilize the structure of the UMSHN and the focus of the ERI Program to increase surveillance for early **kidney disease** particularly in areas of underserved populations with a high predominance of African-Americans. Specific Aim 3: Set up pathways through which individuals with **kidney disease** identified from the statewide surveillance program can link into ongoing studies, educational initiatives and specialized care programs that are all dedicated to narrowing

the racial disparity in **kidney disease** Specific Aim 4: The Renal/Kidney Disease Research Core will establish an effective and enduring infrastructure for sample and data collection that can be utilized for community-based enrollment and examination of individuals participating in ongoing and future trials related to **kidney disease.** The Renal/Kidney Core also has the outstanding participation of Dr. Eve Higginbotham as a Co Investigator. Dr. Higginbotham will participate in the Renal/Kidney Research Core as well as the Shared Resource Core. In the Renal/Kidney Research Core, she will lend her expertise in the area of ophthalmologic disorders, which affect patients at risk for renal disease, patients with renal disease, such as diabetics and hypertensives, or renal patients who have comorbidity such as glaucoma. Dr. Higginbotham and her faculty and staff, Drs. Scott Steidl and Nancy Ellish, will evaluate, in the Shared Resource Core, a novel Teleopthalmology project that may assist renal patients and other types of patients with compliance with recommended guidelines for eye screening.

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

- **Project Title: CORE--TRANSGENIC ANIMAL AND MORPHOLOGY FACILITY**

  Principal Investigator & Institution: Barnes, Jeffrey A.; University of Texas Hlth Sci Ctr San Ant 7703 Floyd Curl Dr San Antonio, Tx 78229

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

  Summary: The Transgenic Animal and Morphology Core is designed to achieve two goals: 1) to provide center investigators and their collaborators services for the generation of transgenic over expressing or knock-out mouse lines and 2) to provide the center investigators and collaborators a morphology component to assess histopathology and phenotypic analysis of transgenic animals and of disease models as outlined in Projects 1,2, 3, 5, and 6. The transgenic animal core will assist investigators in the preparation of a total of two knock-out and one transgenic mouse line. More specifically, the core will assist Dr. Kasinath- Project 2 to generate inducible insulin receptors and Dr. Chen -Project 3 in the deletion of Nek-1. The morphology component will assist investigators in a variety of morphologic techniques including routine light microscopy, immunohistochemistry, dual-label immunohistochemistry, in situ hybridization, electron microscopy, and morphometric quantitation of histological changes using computer assisted image analysis. The morphology core will be heavily used by all investigators in analysis of transgenic phenotype (Projects 2,3,and 5) and in assessment of renal disease in diabetic nephropathy in Humans (Project 1), the baboon (Project 6), rat (Project 5) and mouse (Project 2 & 5); The core will also be instrumental in assessing histopathologic changes in a model of polycystic **kidney disease** (Project 3). Successful attainment of these goals will enhance productivity by the Renal Center participants, recruit new investigators to the study of renal development and pathophysiology, and make available to other renal investigators new tools for the study of **kidney disease.** The Core has an integrated administrative and budgetary structure for the efficient utilization of resources and provisions for an intellectual and educational environment.

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

- **Project Title: CWRU OBRIEN RENAL RESEARCH CENTER**

  Principal Investigator & Institution: Sedor, John R.; Professor; Medicine; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

  Timing: Fiscal Year 2001; Project Start 01-SEP-1998; Project End 31-AUG-2003

Summary: This proposal seeks to establish a CWRU Renal Center. The goal of this Center is to gain a better understanding of the molecular, cellular and genetic basis of kidney failures, laying the groundwork for applications of new methodologies to their treatment. The rationale behind the proposed research program is that a clear delineation of pathophysiological mechanisms is a prerequisite for development of rational treatment strategies. As new drug discovery methodologies are perfected, understanding the molecular basis of renal dysfunction will undoubtedly identify exciting possibilities for treatment of a group of disease with few, effective therapeutic. The Center is composed of five projects, which are linked and supported by a scientific core, the Peptide Biochemistry Core (Core A). Each of the component projects, describe below, addresses the overall goal of the Center. Project 1 (Sendor, Wang) studies mechanisms by which glomerular microenvironment regulates the phenotype of the mesangial cell, which is critically involved in glomerular injury. The goal of Project 2 (Schelling, Haldar) is to define mechanisms of tubular atrophy in progressive **kidney disease** and will test the hypothesis that hypoxia induces Fas-dependent RTC apoptosis. The hypothesis of Project 3 (Brown, Schwalbe) is K+ flux via ROMK is severely compromised in a variant of Bartter's syndrome and proposes that blocking ROMK will be effective treatment and that ROMK blocks will form a new class of diuertics. Project 4 (Iyengar, Sehgal, Olson) capitalizes on a collaborative initiative between members of the Division of Nephrology and the Department of Epidemiology and Biostatistics to collect family history and medical data from affected, relative pairs and families with ESRD to identify genetic risk factors for ESRD. Project 5 (Carlin) propose studies to define elements of the polarized EGF sorting machinery in epithelial cells to better understand the pathogenesis of polycystic **kidney disease.** This Center includes, in addition to nephrologist-scientists, a number of outstanding investigators not previously involved in **kidney disease** research. In summary, the CWRU Renal Center brings together a multi- disciplinary group of investigators to apply state-of-the-art approaches to the analysis and cure of **kidney disease** within the rich research environment of the CWRU School of Medicine.

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- **Project Title: CYSTIC DILATATION OF NEPHRONS IN TRANSGENIC INV MICE**

  Principal Investigator & Institution: Phillips, Carrie L.; Medicine; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, in 462025167

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

  Summary: Polycystic **kidney disease** (PKD) is the most common inherited renal disease, accounting for 5-10% of end-stag renal disease with an annual cost of $240,000,000. The etiology of renal cysts is especially important for the children an adults with inherited PKD who may require dialysis or transplantation for survival. We have a newly describe transgenic mouse model of PKD, called inv/inv, which will be used to conduct studies not possible in humans. The long term goal of this project is to understand how the inheritance of a novel situs inversus gene, inv, results in PKD and loss of renal function. Our general strategy is to study the kidneys of inv/inv mice, which share phenotypic features with autosomal recessive (AR) PKD. They develop situs inversus, PKD and die prematurely from renal failure. The inv gene has been fully cloned and sequenced. Our preliminary data suggest inv is an intracellular protein with discrete localization in specific segments of the nephron. Our experiments will test the hypothesis that the inv gene codes for a developmentally important protein that maintains nephron integrity. Grant funding is a major factor in the PI's immediate goal of attaining research independence and the long-term career goal of becoming a

successful and productive investigator in an academic institution. The specific aims of this present study are as follows: 1. To characterize the inv/inv mouse model of ARPKD, we will perform single and dual photon fluorescence microscopy with cell-specific antibodies and lectins. Immunogold electron microscopy with anti-inv antibodies will target the intracellular localization of the inv protein. These microscopy experiments will allow us to appropriately direct mechanistic studies of inv protein function and interactions. 2. In situ hybridization studies will be used to determine the cellular levels of inv messenger RNA during critical periods of development. This is especially important, as incremental variations in mRNA expression are known to occur during narrow developmental windows. 3. We will use green fluorescent protein-inv constructs and anti-inv antibodies t establish spatial and temporal inv expression patterns during development. We believe the inv/inv model offers a new an exciting opportunity to extend the understanding of the genetic mechanisms of nephrogenesis and the abnormalities in this process which lead to PKD.

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- **Project Title: DATA COORDINATING AND IMAGING ANALYSIS CENTER (DCIAC)**

  Principal Investigator & Institution: Bae, Kyongtae T.; Radiology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 30-NOV-2004

  Summary: Polycystic **kidney disease** (PKD) is a common hereditary disease and ranks fourth as a leading cause of end-stage renal failure. The primary goal of this study is to exploit volumetric imaging methods to identify and quantify morphologic measures that are associated with the PKD stage and the rate of PKD progression. 200 subjects, divided into three cohorts (GFR=30-50, 70- 90 ml/min) will be followed for a four-year period. Two participating clinical centers (PCC) will each contribute data on approximately 100 subjects. Each PCC will collect clinical data and specimens, perform renal functional tests, and obtain MR and US images for each subject at specific follow-up intervals. The data will be delivered or electronically transferred to the data coordinating and imaging analysis center (DCIAC) proposed in this application. Our specific aims are (1) to validate magnetic resonance (MR) volumetric imaging methods for accurate and reliable morphometric assessment of the renal parenchyma and renal/hepatic/pancreatic cysts in PKD patients; (2) to compare morphologic measures obtained from MR imaging data with renal functional measures in PKD patients to determine which morphologic measures are associated with the extent of renal functional impairment and with the rate of disease progression; and structural changes, while considering clinical-effectiveness, cost- effectiveness and patient acceptability. Statistical methods appropriate for growth curve estimation with a heterogeneous population will be developed and applied to characterize the PKD progression for each cohort and for the sample as a whole. The long-term goal of this project is to develop methods that would facilitate shortening the observation period necessary to determine efficacy of treatment interventions in PKD patients.

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

- **Project Title: DATA COORDINATING CENTER FOR PKD TREATMENT NETWORK**

  Principal Investigator & Institution: Miller, J. Philip.; Professor; Biostatistics; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

Timing: Fiscal Year 2002; Project Start 15-AUG-2002; Project End 31-JAN-2009

Summary: (provided by applicant): Washington University proposes to establish the Data Coordinating Center (DCC) for the Polycystic **Kidney Disease** Treatment Network (PKD-TN) within the Division of Biostatistics. WU performs a similar function for the NIDDK-sponsored CRISP study that is developing imaging parameters to follow the progression of Polycystic **Kidney Disease** (PKD). WU generally, and this investigative team specifically, has a strong record of experience as the DCC for multicenter studies. The DCC will participate as a key member of the Steering Committee, taking a leadership role in planning the studies, leading the statistical analyses and reporting of these studies. A web-based data entry system, based on the one currently being used for CRISP, will be customized for the needs of the PKD-TN. The DCC will serve as the communications hub for the PKD-TN, arranging meetings, telephone and electronic communications and producing and archiving study-related documents. A three-group, double-masked, randomized, multicenter, placebo-controlled trial will address whether either an ACE inhibitor or an angiotensenin 2 antangonist will retard the progression of renal impairment in PKD. The trial will enroll 1,800 PKD subjects with a wide range of renal function and follow them for 3-5 years. The primary endpoint will be that of time to death, ESRD or a doubling of the serum creatinine level. GFR levels will be assessed annually with a central laboratory and will be used as a secondary endpoint. The GFR measurements will allow us to address questions about variations in treatment effect according to the severity of renal impairment and the presence of common features of the disease such as hypertension and proteinuria. Blood and urine samples will be collected at baseline and annually and stored in the NIDDK's repository for future pharmocogenitic studies and future studies of biomarkers of the progression of PKD. An early Phase II trial of BMP-7, a cytokine which has an essential role in coordinating the formation of the emerging metanephos, is proposed. BMP-7 has been shown to maintain renal function in animal models with acute and chronic renal disease and to reduce renal hypertrophy. A simple, two-group, placebo controlled, randomized clinical trial will be conducted to determine whether BMP-7 can retard the growth rate of the kidneys in PKD subjects. MRI-based imaging will be used to measure kidney size for the trial.

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- **Project Title: DEVELOPMENTAL GENETICS OF OAK RIDGE POLYCYSTIC KIDNEY GE**

  Principal Investigator & Institution: Murcia, Noel S.; Pediatrics; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-AUG-2002

  Summary: (adapted from the application) Polycystic **kidney disease** (PKD) is characterized by the progressive expansion of multiple cystic lesions, which compromise the function of normal parenchyma. Throughout the course of this disease, aspects of renal epithelial polarity, structure, and function are altered, changing the tubular microenvironment and ultimately causing the formation and progressive expansion of cystic lesions. While the human gene for autosomal recessive PKD (ARPKD) has not been cloned, the gene associated with the Oak Ridge polycystic kidney (orpk) mouse mutation has provided molecular insights into ARPKD. Further genetic analysis of the orpk disease gene, Tg737, has uncovered a critical role for its gene product during early embryogenesis. Unlike the orpk allele, where all homozygotes survive to birth, embryos homozygous for the Tg737-delta2-3-betaGal mutation arrest in development at mid-gestation and exhibit neural tube defects, enlargement of the

pericardial sac and, most notably, left-right asymmetry defects. At mid-gestation the direction of heart looping is randomized, and at earlier stages in development lefty-2 and nodal, which are normally expressed asymmetrically, exhibit symmetrical expression in the mutant embryos. Expression of both Shh and Hnf3beta is down regulated in the midline (floorplate and notochord) at E8.0, indicating that there are significant alterations in midline development in mutants. Additionally, the ventral node cells in mutant embryos fail to express an apical central cilium, which is a characteristic and potentially functional feature of these cells. We propose that loss of Tg737 function in the early embryo causes abnormal or incomplete differentiation of the ventral node epithelium which alters the ability of these cells to properly differentiate as they migrate out of the node and contribute to developing midline structures. A defective midline then causes downstream developmental defects in left-right asymmetry and neural tube development leading to cardiac insufficiency and mid-gestational lethality. The failure of these polarized epithelial cells to properly differentiate in the ventral node of Tg737-delta2-3-betaGal homozygous embryos parallels the abnormal polarity of the EGFR and clonal expansion of principal cells in collecting tubule cysts of the orpk mouse model of ARPKD and in human ADPKD. Analysis of the fundamental cellular defects in ventral node epithelium and their subsequent effects on differentiation and development provides a novel system for investigating the function of the murine ARPKD disease gene Tg737. Knowledge gained from these studies will further our basic understanding and provide novel insight into the fundamental cellular defects in renal tubular epithelium associated with PKD.

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

- **Project Title: ELECTROPHYSIOLOGICAL ANALYSIS OF DROSOPHILA PKD2**

  Principal Investigator & Institution: Lu, Xiangyi; Environmental Health Sciences; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

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

  Summary: (provided by applicant): Much progress has been made recently in understanding the autosomal dominant polycystic **kidney disease** (ADPKD), which affects millions of people world-wild. The main disease phenotype is characterized by the persistent proliferation and de-differentiation of renal epithelial cells that eventually form fluid-filled cysts. Gradually, these cysts cause anatomical distortion and kidney failure. One of the disease-causing genes, PKD2, has a significant overall sequence and structure conservation to various known cation channels. Recent study indicates that expression of PKD2 or a related protein PKDL is sufficient to produce Ca2+-permeable non-selective cation channel activities. Another ADPKD disease gene, PKD1, is also a transmembrane protein that has been shown to interact with PKD2. PKD 1 may regulate PKD2 channel activity which initiates yet undefined intracellular signal transduction pathway that maintains proper epithelial cell polarity, secretion and other functions. This proposal applies newly developed tools of functional genomics to the study of PKD2 gene through its homologue in Drosophila, namely the DmPKD2 gene. We have cloned the DmPKD2 gene and it shows similarities of 48 percent and 59 percent to human PKD2 in two most conserved regions that contain the predicted transmembrane segments. The N- and C-termini of DmPKD2.are more divergent. We propose here to test the hypothesis that DmPKD2 functions as a channel as was shown for other vertebrate PKD2-related proteins. The properties and regulation of DmPKD2 will be quantified. We also propose to test the channel function of DmPKD2 in its native environment, namely living fly epithelial tissues. Specifically, we will genetically over-express or ablate the production of DmPKD2 in culture cells (in vitro) and fly tissues (in

vivo). Single channel analyses will be performed on both the wild-type and mutant cells and tissues where DmPKD2 is normally expressed. The long-term goal of this research is to define the biochemical pathway by which the PKD2 family of channels operates to regulate cell and developmental processes.

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- **Project Title: EPIDEMIOLOGY OF DEMENTIA IN OLDER DIALYSIS PATIENTS**

  Principal Investigator & Institution: Murray, Anne M.; Minneapolis Medical Research Fdn, Inc. 600 Hfa Bldg Minneapolis, Mn 55404

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

  Summary: (provided by applicant): Candidate: Anne Murray, M.D., M.Sc., is a fellowship-trained geriatrician with a Masters in Epidemiology and a staff physician at Hennepin County Medical Center, a teaching hospital affiliated with the University of Minnesota. She is also an investigator with Nephrology Analytical Services, an epidemiology laboratory and repository for the NIH's United States Renal Data System (USRDS) database. Dr. Murray's immediate goal is to pursue research in the epidemiology and prevention of cognitive impairment in dialysis patients. Career Objectives: Dr. Murray's immediate career objectives include: 1) advanced coursework in neuropsychology, study design, longitudinal analysis, and ethical conduct of research, 2) work with her mentors to further develop her research skills in the area of cognitive impairment in renal disease through regularly scheduled meetings and directed readings, 3) conduct a three-year longitudinal study of the prevalence and progression of cognitive impairment in dialysis patients under the guidance of her mentors, 4) continue to conduct analyses on the epidemiology of dementia in dialysis patients using the USRDS database, and 5) during the last year of the award, develop a proposal to obtain funding for a prospective study of the incidence of and risk factors for cognitive impairment in patients with chronic **kidney disease,** formerly called chronic renal insufficiency. Dr. Murray's long-term career objective is to attain independence as an investigator in the area of epidemiology of cognitive impairment in renal disease and other chronic diseases. Research Plan: During the five-year award period, Dr. Murray plans to use findings from analyses of her pilot data and the USRDS database to conduct a prospective longitudinal study of the prevalence and progression of cognitive impairment in dialysis patients in the Twin Cities. The study will test the hypotheses that 1) dialysis patients have a higher prevalence of cognitive impairment than the general population, 2) the risk of cognitive impairment increases with duration in years of dialysis, and 3) age, Modified Mini-Mental State Examination (3MS) score at baseline, education, and history of stroke will be strong predictors of the rate of progression of cognitive impairment in dialysis patients. Subsequently, Dr. Murray plans to collaborate with her mentors to write a major proposal to examine the epidemiology of cognitive impairment in patients with chronic **kidney disease.**

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

- **Project Title: ETIOLOGY OF NEPHROPATHY AND HYPERTENSION IN AASK PATIENT**

  Principal Investigator & Institution: Lipkowitz, Michael S.; Medicine; Mount Sinai School of Medicine of Nyu of New York University New York, Ny 10029

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

  Summary: (adapted from the application) We will study the etiology of hypertension and nephropathy in the majority of the 1094 African-American patients in the African-

American Study of **Kidney Disease** in Hypertension (AASK). The AASK study is an NIH sponsored clinical multicenter trial comparing the effect of two levels of blood pressure control and three antihypertensive regimens on progression of hypertensive nephropathy in African Americans. There is a disproportionate number of African Americans with hypertensive target organ damage, suggesting a genetic susceptibility in this population; paradoxically, few studies have been performed to evaluate such genetic predisposition to disease in this high risk population. The patients of the AASK study offer a unique opportunity to prospectively determine the genetic factors involved in hypertension and hypertensive target organ damage within a high risk and under-studied population. The proposed studies will immortalize white blood cells from patients to provide a renewable source of tissue and DNA from this unique study group, and follow two approaches in assessing the etiology of hypertension, nephropathy, and their sequelae: 1. Studies are proposed to determine whether polymorphisms in candidate genes for hypertension, renal failure, and cardiac disease, including renin-angiotensin system genes, insulin resistance (beta3-adrenergic receptor and lipoprotein lipase) genes, Liddle's syndrome (beta and gammaENaC) genes, and others are related to hypertension or renal failure, severity/rate of progression of renal disease, severity/refractoriness of hypertension, electrocardiographic left ventricular hypertrophy, cardiovascular morbidity and mortality, and overall morbidity and mortality. 2. Additional studies will employ a new technique, mapping by admixture linkage disequilibrium (MALD), which uses the linkage disequilibrium caused by recent admixture of founder populations to localize genes linked to a particular phenotype within a 5-20 centiMorgan region in a genome-wide screen. By utilizing microsatellite markers from the carefully phenotyped patients of the AASK Study it should be possible to identify regions of interest containing genes associated with hypertension, renal failure, and the outcomes described above for candidate genes.

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- **Project Title: GENOTYPE AND PHENOTYPE OF FAMILIAL NEPHROPATHY WITH GOUT**

  Principal Investigator & Institution: Hart, Thomas C.; Associate Professor; Oral Medicine and Pathology; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 15-JUL-2002; Project End 31-MAY-2006

  Summary: (provided by applicant): Familial Nephropathy with Gout (FGN) is a rare kidney disorder characterized by reduced fractional excretion of uric acid, precocious and tophaceous gout, and development of chronic renal failure leading to end-stage renal disease. FGN is transmitted as an autosomal dominant trait, clinical fmdings are variable, response to treatment not predictable and the disease pathophysiology is poorly understood. The goals of this proposal are to identify the gene(s) responsible for FGN and to characterize the clinical manifestations of this condition. We have identified two large families with FGN providing unique opportunities to characterize clinical manifestations and progression of FGN and to identify the gene responsible. Our preliminary studies sublocalize an FGN gene to a 2.0 cM region of chromosome l6p in one family. Linkage data from a second, smaller family is consistent with a broader candidate interval. Additional studies will determine if the same gene is responsible for FGN in both families. The genetic interval we have mapped FGN to is not well characterized. Genetic and physical maps of the region are incomplete and there are no obvious candidate genes for FGN. We propose an integrated clinical and laboratory approach to identify the gene(s) responsible for FGN. We will longitudinally follow

affected family members to better characterize clinical manifestations of FGN (Specific Aim#1). To identify the FGN gene (Specific Aim #2) we propose a hierarchical strategy to 1). Clarify and integrate genetic and physical maps of the candidate interval(s), 2). Continue linkage studies to narrow the candidate interval(s), and 3). Systematically evaluate genes within the interval to identify the gene mutation(s) responsible for FGN in these families. Identification of the specific gene mutation will provide an important discovery that will (a) elucidate important aspects of uric acid tubular transport, (b) provide an understanding of interstitial **kidney disease** and chronic renal failure, and (c) help to better define relationships between hyperuricemia, uric acid excretion, and the development of renal failure. Completion of these studies will permit pre-symptomatic diagnosis for individuals with FGN and enhance our ability to evaluate current treatment strategies as well as to develop new, more effective intervention strategies.

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- **Project Title: HUMAN POLYCYSTIC KIDNEY DISEASE**

  Principal Investigator & Institution: Schrier, Robert W.; Professor; Medicine; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

  Timing: Fiscal Year 2001; Project Start 01-APR-1985; Project End 30-JUN-2006

  Summary: Autosomal Dominant Polycystic **Kidney Disease** (ADPKD) is one of the most common potentially lethal genetic diseases. It occurs worldwide and affects about 1 in 500 to 1000 Americans. The costs for treatment of end- stage renal disease (ESRD) are estimated to exceed 1.5 billion US dollars per year, not including the cost for treatment of other renal and extrarenal manifestations. Over the last 15 years this Program Project Grant (PPG), which is the largest study of ADPKD manifestations in children and adults in the world, has contributed significantly to our understanding of the natural history of this disease. The long-term objective for the competitive renewal is to develop strategies to prevent disease progression. This application focuses on ADPKD kidney and liver disease. Combining a clinical trial with investigations into genetic mechanisms of disease severity and with basic research in an animal model and cell culture systems will be the overall strategy to achieve the goal. The competitive renewal of the PPG continues to take advantage of the unique adult and child population, which has been assembled as a result of the 15-year PPG. This patient population will e used in the first Project-A randomized trial of anti-hypertensive therapy in children, adolescents and young adults with ADPKD- and in the second Project- Identification of modifying gene sin ADPKD. The premise is that identifying genes that promote disease severity will not only help to understand the pathophysiology, but will also allow development of new treatments and section of high-risk patients for treatment trials. The third and fourth will complement the two clinical investigations by performing basic science studies, which have clinical implications for patients with ADPKD. The third Project investigates the role of apoptosis and caspase (apoptosis) inhibitors in the progression to ESRD in the Han:SPRD rat model of ADPKD and in the Pkd2/WS25 mouse model provided by Dr. Somlo, and the fourth Project examines the pathogenesis of hepatic cystic disease. Very little is known about the pathogenesis of liver cysts and thus focused interventions are not possible. Study of the liver will also contribute to our understanding of the factors that cause ESRD in ADPKD.

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- **Project Title: IFN GAMMA AND OTHER MODIFIERS OF KIDNEY DISEASE IN TSC**

  Principal Investigator & Institution: Dabora, Sandra L.; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

  Timing: Fiscal Year 2004; Project Start 01-DEC-2003; Project End 30-NOV-2008

  Summary: (provided by applicant): Renal disease is an important cause of morbidity in tuberous sclerosis complex (TSC), a Mendelian disorder with autosomal dominant inheritance. TSC is a tumor suppressor gene disorder characterized by the development of benign tumors (hamartomas) in multiple organs including the kidneys. Kidney angiomyolipomas are benign tumors consisting of blood vessels, fat cells and smooth muscle cells, and they occur in approximately 75% of TSC patients over the age of 5 years old. Kidney cysts are also common and occur in about 25% of TSC patients. TSC is a genetic disorder with high penetrance but variable expression. Although the variability in expression is not entirely understood, there is recent evidence that some of the variability in renal disease may be explained by modifier genes. It has been shown that high levels of interferon-gamma in TSC mouse models significantly reduce the severity of renal disease in these animals (Hino et al. 2002). It has also been demonstrated that a high expressing allele of interferon-gamma is associated with a decreased frequency of kidney angiomyolipomas in a population of patients with TSC2 mutations (Dabora et al. 2002). TSC is an excellent model disease for investigating the role of modifier genes in genetic disorders causing renal disease. The goal of the projects outlined below will be to further investigate the role of interferon- gamma as a modifier of renal disease in TSC using mouse models, in vitro studies, and genotype/phenotype studies in a large TSC population. Because of the TSC mouse models available for these studies as well as our prior work on genotype/phenotype studies for TSC, we are in a unique position to further define the role of interferon-gamma in this disorder. Furthermore, because interferon-gamma is an approved drug, we will direct significant effort towards testing interferon-gamma as a prevention or treatment agent in preclinical studies using the TSC mouse models. We anticipate that this work will not only improve our understanding of the role of interferon-gamma as a genetic modifier of **kidney disease** in TSC, but will also contribute to the development of novel therapeutic strategies for TSC renal disease and related disorders as well as lead to the identification of novel genetic modifiers.

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- **Project Title: IMPACT OF GENETIC MUTATION OF PKD1 ON RENAL DEVELOPMENT**

  Principal Investigator & Institution: Burrow, Christopher R.; Assistant Professor; Mount Sinai School of Medicine of Nyu of New York University New York, Ny 10029

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-JUN-2008

  Summary: The elucidation of the molecular control mechanisms that regulate tubule morphogenesis during kidney development provides a basis for developing novel therapeutic strategies for the treatment of the group of polycysfic kidney diseases resulting from genetic mutations including ADPKD. A body of evidence suggests that PKD-1 loss of function mutations result in dysfunctional regulation of tubulogenesis in development leading to dilatation of the tubule and formation of cysts. The PKD-1 gene product, polycystin-1 associates with components of the focal adhesion and cell-cell adherens complexes which function via JNK/AP-1 and Wnt/TCF/LEF signal transducfion pathways with impact on regulation of cell proliferation, repression of fetal

gene transcription, cell adhesion and migration. Polycystin-1 is highly expressed in the basolateral membranes of the ureteric bud epithelium of normal developing kidneys consistent with an important role in development and regulation of differentiation of the kidney. We have developed and tested both retroviral and adeno-associated-virus (AAV) vectors for delivery and sustained gene expression in renal cell and organ cultures and plan to develop a series of expression vectors with polycystin-1 mutations for use in primary human renal epithelial cell culture experiments, metanephric kidney organ cultures and transgenic mice to test to develop a rational strategy for design of genetic therapeutic intervention. The aims of this project are: 1. to characterize the biological effects of a series of polycystin-1 mutants on tubulogenesis and the ADPKD cystic phenotype using AAV and retroviral gene delivery into tissue culture cells by transfection and into E11 mouse organ cultures by microinjection into the ureteric bud. 2. to characterize of the biological effects of the selected, most effective polycystin-1 truncation and overexpression mutants in transgenic mice 3. to determine whether re-activation of expression of the wild-type PKD-1 gene at various developmental stages during embryogenesis and postnatal life can ameliorate the course of cystic **kidney disease** using a Cre recombinase null mutant mouse. Important information will gained about mechanism of disease and effectiveness of gene therapy.

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- **Project Title: INTERSTITAL CELL COXS IN RENAL DEVELOPMENT AND DISEASE**

  Principal Investigator & Institution: Hao, Chuan-Ming; Medicine; Vanderbilt University 3319 West End Ave. Nashville, Tn 372036917

  Timing: Fiscal Year 2003; Project Start 23-JUL-2003; Project End 30-JUN-2005

  Summary: (provided by applicant): Of all organs tested, the kidney exhibits the greatest level of expression of the inducible form of cyclooxygenase-2 (COX2) (Guan Am J. Physiol 1997), and within the kidney, the vast majority of COX2 resides in the interstitial cell. The interstitial cell is situated between the renal microvascular and epithelial compartments and so, COX2 derived prostaglandins elaborated by medullary interstitial cells are in an ideal location to modulate the functions of both renal tissues. Accumulating evidence suggests that renal interstitial/stromal cells are involved in virtually all functions of healthy kidney, and in many pathological events of the kidney [Grupp, 1999 #144]. However because COX2 is also expressed in the renal macula densa and COX1 is expressed in the collecting duct, the exact role of these renal interstitial cell COX2 derived prostanoids in the kidney is not precisesly known. The present proposal will focus on the role of renal interstitial/stromal COX mediated prostanoids in normal and diseased kidney including diabetic and polycystic **kidney disease.** Elucidating the bio-activity of renal prostaglandins will be important not only in understanding the maintenance of normal renal function but also in determining their potential as therapeutic targets in disease. The proposed studies will have two specific aims: Specific Aim 1: Generating and characterizing renal interstitial cell selective COX2 deficient mouse. Conventional COX2 gene disruption results in kidney dysgenesis, suggesting COX2 plays an important role in the kidney development, it remains uncertain whether interstitial or epithelial (i.e. nacent macula densa) derived COX2 is necessary for normal renal development. Futhermore examination of the role of COX2 in the adult COX2 null mouse is complicated by this renal dysgensis. Conditional COX2 knockout mice will allow this problem to be circumvented. Furthermore, the conditional COX2 knockout mouse will make it possible to study selectively the role of renal interstitial cell COX2 in the kidney. Specific Aim 2: Examine the role of renal interstitial COX2 and COX1 in

maintenance of normal function and in the pathogenesis of disease such as diabetic nephropathy and polycystic **kidney disease.** The proposed studies will examine the effect of selective renal interstitial cell COX2 deletion on the (1) ability of renal papilla to survive hypertonic stress; (2) development of diabetic **kidney disease;** (3) on rate of expansion of cyst.

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- **Project Title: KANSAS INTERDISCIPLINARY CENTER FOR PKD RESEARCH**

  Principal Investigator & Institution: Grantham, Jared J.; Distinguished Professor; Biochemistry; University of Kansas Medical Center Msn 1039 Kansas City, Ks 66160

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2004

  Summary: OVERALL (Taken directly from the application) Polycystic **kidney disease** is observed throughout the animal kingdom. In humans it frequently leads to renal failure. It is widely believed that the destructive consequences of this group of diseases rest in the development of cysts within renal tubule segments and their growth to enormous size. The Kansas Interdisciplinary Center for PKD Research will build-on a rich history of basic and clinical polycystic **kidney disease** research at this site to address important questions about the molecular and cellular pathogenesis of cyst development and growth. The theme of this Center application is "Polycystin and signal transduction in polycystic kidney disease". Four established PKD investigators and one established researcher new to this field are Principal Investigators of five research projects. An administrative Core will include a pilot and feasibility study by an established molecular biologist who is new to the field. All of the projects are explicitly linked to the study of polycystic **kidney disease** and range from studies of polycystin mutations in lower organisms to the molecular mechanisms by which cysts develop and progressively enlarge in mammals. Lower animals serve as a road map to functions that are highly conserved in the biologic kingdom. Project 1 will determine the patterns of expression and comparative functions of two cyst-forming genes, CePKD-2 and CeTg737, in C. elegans. Project 2 will establish a model of polycystic **kidney disease** in Drosophila in order to reconstruct the network of molecular events in the PKD1/PKD2 mediated pathway. Project 3 will test the hypothesis that PKD1 functions as a G-protein coupled receptor that when mutated disturbs early embryological development and the development of the kidney and other organ systems. Project 4 will test the hypothesis that polycystin-1 regulates signal transduction pathways that modulate the activity of glucocorticoid receptor using the glucocorticoid-induced expression of the renal glutathione S-transferase Ya gene as a model system. Project 5 will test the hypothesis that in ADPKD, renal cyst enlargement is accelerated by elevated levels of intracellular cyclic AMP that, through the activation of protein kinase A, stimulates other cellular mechanisms, most notably the ERK/MAP kinase pathway. Project 6 will test the "second hit" hypothesis as a mechanism for the onset of polycystic **kidney disease** by producing mice containing both a primary mutation in PKD 1 and an inducible second-hit somatic mutation in the other allele. The long term goal is for this research to contribute to novel treatments to slow or arrest the progression of polycystic kidney disorders.

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- **Project Title: KIDNEY DAMAGE IN MURINE LUPUS**

  Principal Investigator & Institution: Singh, Ram R.; Associate Professor; Internal Medicine; University of Cincinnati 2624 Clifton Ave Cincinnati, Oh 45221

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

Summary: (provided by applicant): Lupus nephritis is believed to result from glomerular deposition of immune complexes, triggering local kidney inflammation, followed by worsening glomerulosclerosis and end stage renal disease. The mechanisms responsible for this chronic **kidney disease** progression are poorly understood. Several reports and our preliminary data suggest a link between decreases in T cell production of transforming growth factor beta (TGFbeta) with autoantibody production, and increases in renal TGFbeta expression with the development of chronic kidney lesions. The central hypothesis of this proposal is that TGFbeta plays dual roles in the development and progression of lupus nephritis: while decreased TGFbeta levels promote early stage lupus nephritis by enhancing T and B cell activation and autoantibody production, increased TGFbeta levels accelerate late stage **kidney disease** by inducing increased extracellular matrix production. The proposed studies will evaluate changes in the expression levels of TGFb, its receptors and signaling proteins in the lymphoid and renal tissues during progression of **kidney disease** in murine models of lupus. These studies will build on preliminary data indicating that urine TGFbeta levels rise in response to increases in TGFbeta activity in lupus kidney cells, thus serving as a diagnostic marker for chronic kidney damage. The proposed studies will also investigate the potential mechanisms of renal TGFb overexpression in lupus, and more importantly, determine the contribution of the TGFbeta system to autoantibody production and kidney damage. TGFbeta blockade in vivo using monoclonal antibodies will be investigated as a potential therapeutic approach that could inhibit or reverse the development of chronic kidney lupus disease, without worsening autoimmunity. Our broad goals in this proposal are to understand the mechanisms of kidney damage in lupus. Relevant to the current RFA, this proposal will: a) identify a diagnostic marker (e.g., urine TGFbeta levels) that will allow prediction of the progression of disease in target organs, b) make use of novel conditional, tissue-specific TGFb signaling knockout mice to investigate the mechanisms that cause matrix deposition and tissue damage, and c) explore alternative treatment strategies for preventing organ damage in lupus.

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- **Project Title: KIDNEY DISEASE IN CHILDREN DATA MANAGEMENT AND ANALYSIS**

  Principal Investigator & Institution: Munoz, Alvaro; Associate Professor; Epidemiology; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

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

  Summary: (provided by applicant): The number of cases of ESRD in the US is expected to more than double by the year 2010. In order to develop effective interventions, a description of the natural history of Chronic **Kidney Disease** in children is needed. A prospective cohort study is optimal to achieve the scientific goals to better understand the progression of **kidney disease** and its consequences on neurocognitive development, growth and risk factors for cardiovascular disease. The purpose of this application is to establish the Data Coordinating Center for the prospective study of **Kidney Disease** in Children. We will provide leadership in data management, study coordination, and analytical methodology and thereby enhance the scientific scope of the proposed study. The Specific Aims are to: 1) provide biostatistical and epidemiologic expertise for the design of the overall cohort study to achieve its scientific goals; 2) provide an infrastructure to coordinate and conduct the study including: establishment of central laboratories and links to a central repository under the auspices of the NIDDK; the development and revision of study protocols; tracking of ongoing study-

wide research; facilitation of communication among committees and working groups 3) manage the data collected in the study using a web-based data management system for entering, editing, merging, storing and backing up data; 4) provide biostatistical and epidemiological leadership in the analysis, interpretation and presentation of study-wide initiatives and develop novel statistical and epidemiological methodology applicable to the scientific research initiatives of the study; 5) implement a quality assurance program that integrates expertise in data management, study coordination, statistical methodology and scientific disciplines. Our proposed center will be the KIDMAC (Kidney Disease in Children Data Management and Analysis Center). We propose that we direct the Data Management, Analysis and Quality Control subcommittee as well as actively participate in the Steering and other committees according to the organizational mechanisms established by the study. KIDMAC will closely interact and provide reports to the External Advisory Committee. KIDMAC will procure hardware and develop software needed to carry out the management and analysis of the data. In coordination with the Steering Committee, KIDMAC will implement procedures (e.g., a public data tape) to share data with external investigators.

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- **Project Title: KIDNEY DISEASE/HYPERTENSION IN AFRICAN AMERICANS-DCC**

  Principal Investigator & Institution: Gassman, Jennifer J.; Biostatistician; Cleveland Clinic Foundation 9500 Euclid Ave Cleveland, Oh 44195

  Timing: Fiscal Year 2003; Project Start 15-AUG-1994; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of reno-protective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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- **Project Title: MECHANISMS OF ABERRANT EGF RECEPTOR SORTING IN POLYCYSTIC KIDNEY DISEASE**

  Principal Investigator & Institution: Carlin, Cathleen R.; Professor; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

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

  Summary: Formation of epithelial cell polarity is a fundamental process in embryonic development and organogenesis. Polarized epithelia in adult animals form a physical barrier between the host and external environment essential for homeostasis. Polarized epithelia maintain distinct apical (Ap) and basolateral (BL) membrane domains, by actively regulating membrane distribution of lipids and proteins as well as the sub-membranous cytoskeleton unique to each surface. Many questions remain about how membrane polarity is achieved, chief among them how Ap and BL proteins are packaged in distinct transport vesicles at the trans-Golgi- network (TGN). Sorting of BL proteins is mediated in part through recognition of distinct cytoplasmic sorting signals that also appear to regulate polarized sorting in endosomes. Although many BL sorting signals have common features, consensus motifs have not emerged, making it unclear whether all BL signals mediate transport by the same or different pathways. We propose to address this question by studying a novel autonomous Bl signal which we have identified in the EGF receptor (EGFR). This signal is located between residues K652 to A674 in the EGFR juxta- membrane domain, and mediates BL transport of cytoplasmically truncated EGFRs and protein chimeras containing a luminal. This BL signal critical tyrosine and leucine residues and do not overlap any of the known EGFR endocytic signals, features that distinguish it from many other well- characterized BL sorting signals. Computer modeling suggests a propensity for this region to form an amphipathic helix, in contrast to other BL signals whose critical structure suggests a propensity for this region to form a amphipathic helix, in contrast to other BL signals whose critical structure in a beta-turn. This region also induce T654, a known substrate for protein kinase C, raising the possibility that its activity is regulated by phosphorylation. Immediate goals are to understand the mechanism by which this signal establishes and maintains EGFR' polarity. A long-term goal is to understand how genes which cause polycystic **kidney disease** alter this process, since non-polar EGFR expression is a common finding that renal cysts both in humans and animals disease models. The specific aims will: test the hypothesis that BL sorting of cytoplasmically truncated EGFRs is critically dependent on particular amino acids in the BL signal; test the hypothesis that residues K652 to A674 regulate BL transport of full-length EGFRs; test the hypothesis that residues K652 to A674 regulate polarized sorting in endosomes; and characterize elements of the EGFR sorting machinery by identifying proteins that interact with EGFR residues K652 to A674.

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

- **Project Title: MODEL OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE**

  Principal Investigator & Institution: Zhou, Jing; Associate Professor; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

  Timing: Fiscal Year 2001; Project Start 30-SEP-1995; Project End 30-NOV-2004

  Summary: The applicant's long-term objective is to understand the pathophysiology of autosomal dominant polycystic **kidney disease** (ADPKD) as a basis for rational therapy, including gene therapy, of the disease. Recent studies have shed considerable light on the genetic basis of ADPKD. Mutations in PKD1 account for approximately 90 percent of

cases. PKD1 encodes a cell-membrane protein, 'polycystin-1', that is most abundantly expressed in various tissues, including the kidney, during embryonic development. One of the most powerful approaches for the study of disease pathogenesis is targeted gene mutation. Standard transgenic technology results in insertion of the transgene at quasi-random sites in the genome so that the transgene and endogenous genes are simultaneously expressed. Gene targeting, by contrast, allows a mutant sequence to be substituted for the allelic endogenous sequence so that the mutation can be studied in the context of the natural chromosomal (regulatory) environment. Two different targeted mutants of Pkd1, the mouse homologue of PKD1, have recently been generated in the P.I.'s laboratory. Homozygotes develop severe polycystic kidney and pancreatic disease and die in the perinatal period. Heterozygotes develop scattered focal renal cysts throughout the kidneys and liver in a manner reminiscent of human ADPKD. The major goal of this proposal is to use these animals to identify the pathways that lead from polycystin-1 mutation to cyst formation. These animals will also be used to test existing hypotheses of cyst formation, including the role of apoptosis and the stimulation of EGF receptors abnormally localized on the apical surfaces of cyst lumens. Tissue- and stage-specific Pkd1-mutants will also be generated using the Cre-loxP system. Targeted mutant mice provide authentic models of human PKD1-disease that can be used to develop and evaluate new therapies for ADPKD. Such studies are much harder to perform in ADPKD patients because of the gradual progression of the disease in man and significant ethical and safety concerns.

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

- **Project Title: MOLECULAR ANALYSES OF TWO MOUSE KIDNEY DISEASE MODELS**

  Principal Investigator & Institution: Davisson, Muriel T.; Senior Staff Scientist; Jackson Laboratory 600 Main St Bar Harbor, Me 04609

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

  Summary: (provided by applicant): Over 600,000 people in the U.S. suffer from kidney diseases; more than 50,000 die each year. Mouse models are the paradigm for characterizing the etiology and pathogenesis of kidney diseases. The purpose of this project is to identify the mutated genes in two novel mouse models for **kidney disease.** Bilateral polycystic kidneys (bpck) is a spontaneous recessive mutation that causes classic polycystic **kidney disease.** It is a new model because it maps to a region of the mouse genome that has no other **kidney disease** gene. Based on conserved homology, bpck will likely indicate a new human polycystic **kidney disease** gene. Variable hydronephrosis (vhn) is a recessive mutation caused by one of the breakpoints of a reciprocal translocation. vhn presents uni- or bilateral hydronephrosis and renal agenesis/dysgenesis. Preliminary genetic analyses indicate that each of the phenotypes is caused by mutation in a single major gene. Aim 1 is to refine the chromosomal positions of the mutations with a high resolution genetic intercross for bpck and BAC/FISH physical mapping for vhn. Aim 2 is to identify the mutated genes using the positional candidate gene approach and standard molecular protocols. Human orthologues and gene locations will be predicted from the results. Aim 3 is to analyze in detail the disease phenotypes and progression. Gene expression patterns will be determined by TISH and protein localization by immunochemistry. Aim 4 is to analyze gene function by identifying interacting genes using microarrays and quantitative RT-PCR.

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

- **Project Title: MOLECULAR GENETICS OF C ELEGANS RENAL TUBULES**

  Principal Investigator & Institution: Buechner, Matthew J.; Assistant Professor; Microbiology; University of Kansas Lawrence Lawrence, Ks 66045

  Timing: Fiscal Year 2001; Project Start 01-SEP-1998; Project End 31-AUG-2003

  Summary: (Adapted from the Applicant's Abstract): Polycystic **kidney disease** is one of the most common human genetic conditions, and causes the slow swelling of cysts within a subset of nephrons over the course of years, which eventually results in loss of nephritic function and end- stage renal disease. The genes most often mutated in this disease have been sequenced, but it is not clear how the normal proteins act to maintain the narrow tubular structure of the nephron, as well as other similar structures such as hepatic ducts. Several theories exist as to the root cause of polycystic **kidney disease,** but are difficult to prove, in part because there is not model extant where the initial stages of cystogenesis can be studied. The nematode Cae norhabditis elegans offers such a model. It possesses rudimentary renal tubules, the excretory canals, that can be observed in living organisms during embryogenesis. I have isolated and characterized mutants in 12 genes that cause a novel phenotype, designated Exc, in which the excretory canals form large cysts that are formally analogous to the polycystic nephrons of vertebrates. This application proposes a detailed molecular study of the function of four exc genes and their products. The genes have been chosen based on the variety of their phenotypes, and on genetic interactions with each other and with known cytoskeletal compounds. The four exc genes will be cloned by microinjection of wild-type DNA into mutant worms, and their cDNA sequences determined. The four genes will then be tagged by linkages to the gene encoding the auto-fluorescent protein GFP, and injection to form transgenic worms. By observation of the site and time of organismal development where fluorescent protein appears, They will deduce where and when these proteins normally function, at both the organismal and subcellular levels. Finally, these four exc genes will be tested via yeast two-hybrid assay for the ability to bind to each other and tpo known cytoskeletal components directly. These experiments will provide a detailed framework for understanding the range of cytoskeletal structures necessary for maintaining a narrow tubular structure, and how that structures can be deranged to form large cysts both in model organisms and in humans.

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

- **Project Title: MOUSE MODELS OF POLYCYSTIC KIDNEY DISEASE (PKD2)**

  Principal Investigator & Institution: Somlo, Stefan; Associate Professor; Internal Medicine; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2001; Project Start 15-JUN-1998; Project End 31-MAY-2003

  Summary: (Adapted from the Applicant's Abstract): "The primary interest of our research is unraveling the pathogenesis of polycystic **kidney disease.** To this end, they have used positional cloning to identify the second gene for human autosomal dominant polycystic **kidney disease** (PKD2). The current proposal centers on the hypothesis that genetically altering the murine homologue of the PKD2 gene, Pkd2, will enable us to produce animal models whose phenotypes are faithful to those of human autosomal dominant polycystic **kidney disease** (ADPKD). They have produced a mouse line with a targeted mutation in which the first coding exon of Pkd2 has been disrupted. Mice heterozygous and homozygous for this allele develop polycystic kidneys and livers that recapitulate the human disease phenotype. The disease develops faster in homozygotes. They propose histopathological and functional characterization of the

renal and extra-renal phenotypes of these mutant mouse lines as well as further analysis of the molecular consequences of the gene targeting event. This murine model of ADPKD has some residual polycystin-2 expression in the homozygous state. They propose to create a model in which exons 1, 2, and 3 of Pkd2 have been deleted. These null mice will provide a model system for studying the phenotype. In addition, they propose to introduce naturally occurring premature termination codons found in human families with ADPKD, into Pkd2. They will characterize the ensuing mouse phenotypes in heterozygous and homozygous mice and will characterize the functional consequences, at the level of the protein product, of these truncating mutations. Finally, they plan to study the effects of factors other than germ line mutation in Pkd2 on the occurrence and progression of the renal and extrarenal manifestations in mouse models of ADPKD. They will use marker assisted breeding strategies to produce congenic strains bearing mutations in Pkd2 on different genetic backgrounds. They will investigate the effects of defects in DNA mismatch repair on the progression of ADPKD by breeding Pkd2 mutations onto a MLH1-deficient mouse line."

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

- **Project Title: NIDDK BIOTECHNOLOGY CENTER**

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

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-AUG-2003

  Summary: (Abstract of the application) The use of microarray technologies for transcriptional profiling has revolutionized the approach for characterizing the pattern of gene expression in cells under physiological and pathological conditions. The goal of this NIDDK Biotechnology Center is to build a comprehensive integrated microarray facility that will allow N1DDK researchers to create and analyze customized and commercial expression arrays as tools to gain new insights into disease pathogenesis and mechanisms, as well as permitting the characterization of the functional and regulatory pathways of disease related genes. Results from these studies will ultimately be applied for diagnosis, drug screening and treatment selection for diverse human disease states. We capitalize on the existence of a unique group of NIDDK funded investigators in the Harvard community and on the research, teaching and clinical strengths of the Beth Israel Deaconess Medical Center (BIDMC), Joslin Diabetes Center (JDC), Children's Hospital, Dana Farber Cancer Institute(DFCI) and other Harvard Institutions to create a multi-institutional NIDDK Biotechnology Center. This grant application focuses particularly on the strength of the combined diabetes, obesity, and nephrology programs at our institutions which are reflected in the selection of the 10 ongoing and 3 feasibility projects. A critical component of the Center, in addition to the Technology Core, is the inclusion of a highly interactive Bioinformatics Core. One of the strengths of the Center will be the unique capacity to provide web-accessible annotation, cataloging facilities and state-of-the-art bioinformatics analyses to all NIDDK investigators. This will enable researchers from all Projects to maximally utilize the expression data sets to determine functional dependencies among the known genes and Expressed Sequence Tags (ESTs) and direct further biological validation of these putative dependencies. The NIDDK Biotechnology Center will be organized into several Cores: the Technology Core, the Bioinformatics Core, and the Education Core which will be supervised and coordinated by the Administrative Core. The NIDDK Biotechnology Center will combine the complementary technologies of Affymetrix oligonucleotide microarray technology, custom made microarrays, and real time PCR with bioinformatics, and focus this expertise on problems in diabetes, obesity, and **kidney**

disease. Knowledge gained from these investigations should provide insights into regulatory pathways and mechanisms of disease pathogenesis involved in diabetes, obesity and **kidney disease.** Finally, the Center will provide novel educational programs to attract other NIDDK researchers to microarray technologies and to disseminate knowledge gained by the investigations.

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

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

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

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

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

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

- **Project Title: OXIDATIVE STRESS IN CHRONIC KIDNEY DISEASE**

  Principal Investigator & Institution: Himmelfarb, Jonathan; Professor; Maine Medical Center 22 Bramhall St Portland, Me 04102

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

  Summary: (provided by applicant): The broad goals of this proposal are to develop enhanced understanding of how the progressive loss of kidney function leads to increased oxidative stress, inflammation, and accelerated development of cardiovascular disease. The long-term objective of this proposal is to develop the data critical for a subsequent large scale, multicenter, randomized, controlled trial designed to alleviate oxidative stress, reduce inflammation, and reduce cardiovascular morbidity in patients with chronic **kidney disease.** Currently, both the incidence and prevalence of chronic **kidney disease** leading to end-stage renal disease continue to increase at an alarming rate in the United States. According to the United States Renal Data System, in 2000 there are 370,000 prevalent ESRD patients, which are expected to grow to 610,000 by the year 2010. Furthermore, the adjusted death rate for all incident ESRD patients was 19.8 per 100 patient years at risk, with cardiovascular disease accounting for more than 50 percent of mortality in this patient population. Recent analyses demonstrate that there are at least 10.9 million people in the United States with chronic **kidney disease** and that

for this population, there are substantially increased cardiovascular risks, prompting the Surgeon General to include chronic **kidney disease** s a focus area for improving the nation's health in Healthy People 2010. The metabolic derangements accompanying progressive loss of kidney function lead to unique patterns of oxidative injury specific to the uremic state. For patients with chronic **kidney disease,** non-traditional risk factors for cardiovascular disease such as increased oxidative stress and inflammation may be especially important. The aims of this proposal are to determine, in a prospective study, how progressive loss of kidney function influences oxidative stress, inflammation, and cardiovascular disease, and how oxidative stress, inflammation, and endothelial dysfunction are interrelated. A further aim is to determine in the longitudinal study is to determine the extent to which increased oxidative stress and inflammation are risk factors for cardiovascular disease events in patients with chronic **kidney disease.** An additional aim is to determine the effects of antioxidant therapy on biomarkers of oxidative stress, markers of inflammation and endothelium-dependent vascular function in patients with chronic **kidney disease.** This proposal incorporates a series of observational and interventlonal studies measuring the extent of cardiovascular disease with extensive ex vlvo measures of biomarkers of oxidative stress and inflammation in patients with chronic **kidney disease.** Coordination between the clinical data and the ex vivo studies will be emphasized to achieve maximal understanding of the pathophysiology of uremic cardiovascular disease.

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

- **Project Title: PATHOGENESIS OF SICKLE CELL GLOMERULOPATHY**

  Principal Investigator & Institution: Guasch, Antonio; Medicine; Emory University 1784 North Decatur Road Atlanta, Ga 30322

  Timing: Fiscal Year 2001; Project Start 01-SEP-1998; Project End 31-JUL-2003

  Summary: (Adapted from the Applicant's Abstract): In addition to well-described renal tubulointerstitial damage, sickle cell anemia (SSA) may cause proteinuria and progressive renal insufficiency, leading to end-stage renal disease. They have shown that this results from a unique type of glomerulopathy, characterized by a distinctive set of glomerular hemodynamics and glomerular macromolecular permeability characteristics. They propose to determine: (1) genetic factors and clinical markers that identify patients who will develop this complication; (2) the mechanisms underlying the glomerular injury; and (3) whether blockade of the renin-angiotensin system is beneficial in patients who have progressive renal insufficiency. They have shown that albuminuria is a sensitive marker of a glomerulopathy in SSA patients, and that microdeletions at the a-globin gene locus protect from sickle glomerulopathy. Thus, they will screen children and adult SSA patients for increased levels of albuminuria to determine the prevalence of glomerular involvement in SSA and its usefulness as a predictive marker for late renal insufficiency, and they will determine mechanisms of renal protection by the a-globin microdeletions. They will determine the role of the nitric oxide system in mediating the glomerular dysfunction by blocking experimentally its formation, and the role of the renin-angiotensin system in progressive renal insufficiency by experimentally blocking angiotensin II formation and determining whether certain regulatory elements in the angiotensin converting enzyme (ACE) gene, a key enzyme in the formation of angiotensin, are associated with a more severe form of **kidney disease.** They will analyze with immunohistological and morphometric methods kidney biopsies of patients with sickle glomerulopathy to determine the glomerular substructures that are damaged in this disease. They hope that this

information will help design trials that target patients at higher risk and find new treatments for this disease.

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

- **Project Title: PATHOPHYSIOLOGY OF ARPKD: ROLE OF ABERRANT TRANSPORT**

  Principal Investigator & Institution: Satlin, Lisa M.; Professor; Pediatrics; Mount Sinai School of Medicine of Nyu of New York University New York, Ny 10029

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

  Summary: The hereditary forms of polycystic **kidney disease** (PKD) include the common autosomal dominant form (ADPKD), affecting 1 in approximately 1000 of the population, and the less common autosomal recessive form (ARPKD), affecting 1 in approximately 20,000 live births. Both diseases are characterized by the formation and expansion of cysts derived from specific segments of the nephron. In ADPKD, the gradual destruction of normal renal parenchyma by cysts arising in multiple nephron segments lead to renal failure in approximately 50% of patients by the sixth decade of life. ARPKD, a disease with high infant morbidity, is characterized by the progressive dilatation of collecting ducts, the nephron segment responsible for the final renal regulation of Na, K, acid-base and water balance. Three mechanisms have been implicated in the process of cyst formation and expansion: cell proliferation, abnormal extracellular matrix and adhesion, and net transepithelial fluid. Whereas data exists to implicate the former two processes in the pathogenesis of ARPKD, little is known about the regulation of transepithelial solute and water transport in this disease. Our long term goal is to identify alterations in the expression and regulation of epithelial cell transport pathways that contribute not only to cyst expansion, but also the early onset of hypertension and polyuria in APRKD. The hypotheses we propose to examine in this 5-year application are focused on (I) characterizing the molecular and functional expression of ion channels, transporters, and receptors, and (II, III) exploring the mechanisms by which aberrant autocrine/paracrine signaling and/or cellular responses to biomechanical forces lead to dysregulated transepithelial transport in ARPKD collecting dust cysts. To best understand the pathogenesis of human disease, we propose to perform most studies described in this application in immortalized principal cell lines derived from human ARPKD collecting duct cysts or age-matched normal human kidney (NHK). Parallel studies will also be performed in the orpk murine model of ARPKD, whose microdissected tubules can be isolated and microperfused in vitro.

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

- **Project Title: PATHOPHYSIOLOGY OF RECESSIVE POLYCYSTIC KIDNEY DISEASE**

  Principal Investigator & Institution: Avner, Ellis D.; Professor; Pediatrics; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2004

  Summary: OVERALL (Taken directly from the application) The overall objective for the development of an Interdisciplinary Center for Polycystic **Kidney Disease** Research at Case Western Reserve University (CWRU) is to attract a partnership of interdisciplinary research among investigators who will use complementary and integrated approaches to study the molecular and cellular pathophysiology of autosomal recessive polycystic **kidney disease** (ARPKD). ARPKD has an incidence of 1: 10,000 to 1: 40,000, has a mortality of 40-65% in the newborn period, and accounts for approximately 5% of all

end-stage renal disease in children. Other than end-stage renal disease therapy and palliative measures designed to treat the complications of progressive portal hypertension, there is no known therapy for progressive renal cyst formation and enlargement or progressive biliary ectasia and fibrosis in ARPKD. Therefore the overall goal of the Center is to support scientific investigation directed at delineating the fundamental aspects of the disease process which will translate into the design of preventative and/or curative strategies for ARPKD. An ancillary objective of the Center is to attract new scientific expertise to the study of polycystic **kidney disease.** To achieve the stated objectives of the Center, the program involves a interdisciplinary research team drawn from the Departments of Pediatrics, Genetics, and Physiology & Biophysics at CWRU. The three Projects, three Cores, and two Pilot and Feasibility studies are scientifically integrated into an overall scheme which follows directly from current understanding of the molecular and cellular pathophysiology of ARPKD. Project 1, "Epithelial Growth Factor Mislocalization in ARPKD" focuses on a key process mediating abnormal epithelial cell proliferation. Project 2, "Altered Collecting Tubule Ion Transport in ARPKD" focuses on abnormalities in key ion transport processes which mediate altered tubular fluid secretion. Project 3, "Pharmacological and Genetic Therapy of ARPKD" is a translational project to develop therapeutic strategies which target key processes operative in the development and progression of disease. To support the scientific program, an Administrative Core will coordinate Center activities and specifically focus on maximizing scientific interactions of Center Investigators while monitoring and critically evaluating scientific process and encouraging new research in polycystic kidney disease-related areas. A Transgenic & Animal Resource Core will facilitate whole animal experimental approaches for all projects of the Center using state-of-the-art molecular genetic technology. A Cell Culture Core will provide and maintain primary cells and cell lines from human and murine control and cystic kidneys for the proposed studies. Though largely focused on the molecular and cellular pathophysiology of ARPKD, much of the basic knowledge and many of the treatment strategies developed by the Center will also have relevance to the study and treatment of autosomal dominant polycystic **kidney disease.**

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- **Project Title: PATIENT ORIENTED RESEARCH IN KIDNEY DISEASE**

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

  Timing: Fiscal Year 2001; Project Start 15-MAY-1999; Project End 31-MAR-2004

  Summary: (adapted from the application) Neil R. Powe, M.D., is Associate Professor of Medicine and Director of the Welch Center at the Johns Hopkins University School of Medicine. He holds a joint appointment in the Department of Epidemiology at the Johns Hopkins School of Hygiene and Public Health where he is Director of the Clinical Epidemiology Program. He is seeking this Midcareer Award in Patient-Oriented Research to concentrate his effort in clinical research in **kidney disease** and build the training program in **kidney disease** research. Dr. Powe has conducted several clinical investigations in nephrology over the past 12 years including a study of the effectiveness of recombinant human erythropoietin for treatment of anemia of ESRD (end stage renal disease), a study of the incidence, risk factors and prognosis of septicemia in ESRD patients, a study of co-morbid cardiovascular disease in ESRD patients, a study of the natural history and risk factors for ESRD among patients with diabetes mellitus, a study of the impact of dialysis care deficiencies on patient mortality and hospitalization, a study comparing physical examination with color flow Doppler for detection of vascular

access failure and a randomized clinical trial and observational studies of high versus low osmolality contrast media-induced nephrotoxicity. Dr. Powe directs the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) study. This is a national prospective cohort study comparing peritoneal dialysis and hemodialysis and a large versus small dose of dialysis. The study now has over 1034 patients enrolled making it one of the largest and most representative prospective cohorts of dialysis patients ever studied in the U.S. Data on medical history, laboratory studies, co-morbidity and severity of disease and clinical outcomes are being collected. The study has also established a specimen bank which provides exciting opportunities for studies examining both the etiology and consequences of **kidney disease** or its treatment. Dr. Powe has mentored a cadre of trainees and junior faculty in clinical research in **kidney disease.** This award will permit Dr. Powe to make even a greater contribution to patient-oriented research in nephrology, concentrating his efforts and helping him produce future clinical scientists who are rigorously prepared to becomes independent investigators in **kidney disease** research.

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- **Project Title: PAX2 INTERACTING PROTEINS IN DEVELOPMENT AND DISEASE**

  Principal Investigator & Institution: Dressler, Gregory R.; Associate Professor; Pathology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2003; Project Start 15-JAN-1999; Project End 31-MAR-2007

  Summary: (provided by applicant): Understanding the genetic basis of mammalian development is not only important from a basic biological view but is also relevant to human disease. The development of the mammalian embryo from a single fertilized egg utilizes the entire spectrum of genetic and biochemical regulatory mechanisms. Pluripotent precursor cells, or stem cells, must proliferate to renew the embryonic population and also differentiate to generate the highly specialized cell types unique to particular tissues and structures. Many types of human diseases result from the aberrant proliferation of cells that appear more de-differentiated, assuming an embryonic phenotype. In cancer, such dedifferentiated cells are also prone to migration and invasion, two processes oft seen in the developing embryo. Growth and differentiation of precursor cells are controlled both by intrinsic proteins, such as transcriptional activators and repressors, and by extrinsic factors, such as secreted cell signaling molecules. The interplay between cell-cell signaling and gene activation by transcription lies at the heart of genetic regulatory mechanisms controlling differentiation, proliferation, cell death, and morphogenesis. The developing kidney is an excellent model system to study epithelial cell differentiation and morphogenesis of a complex organ system. Pax2 is a transcription factor transiently expressed in the early kidney precursor cells, the metanephric mesenchyme, and in the proliferating epithelial derivatives of this mesenchyme. While Pax2 is absolutely essential for kidney development, failure to suppress Pax2 expression in more differentiated renal tubules is associated with a variety of disease including renal cell carcinoma, polycystic **kidney disease,** and juvenile cystic dysplastic kidneys. The activity of Pax2 is stimulated by phosphorylation of the transactivation domain by the c-Jun N-terminal kinase (JNK). Furthermore, the interaction of Pax2 with the Groucho family of transcriptional repressor molecules inhibits phosphoprylation of the Pax2 activation domain. Thus, Pax2 activity is regulated by both extrinsic signaling, through JNK, and by intrinsic nuclear factors, such as Groucho, to control the activation or repression of downstream Pax2 target genes. This proposal will map the specific serine residues of Pax2

phosphorylation within the large activation domain. Phospho-Pax2 specific antibodies will be generated to localize the active form of the Pax2 protein in vivo and to determine the interactions of Phospho-Pax2 with the cellular transcription machinery. We will also address the role of the Pax2 interacting protein PTIP in modulating Pax2 activity. PTIP is an essential nuclear factor for cell proliferation that associates with actively expressed chromatin. Given the role of Pax2 in the proliferation of renal epithelial cells and in renal disease, controlling Pax2 activity through its interactions with other cellular proteins can potentially lead to novel therapeutic interventions for cancer, PKD and other **kidney disease.**

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- **Project Title: PILOT STUDY--GENETICS OF DIABETIC NEPHROPATHY IN BABOON**

  Principal Investigator & Institution: Rincon-Choles, Hernan; University of Texas Hlth Sci Ctr San Ant 7703 Floyd Curl Dr San Antonio, Tx 78229

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

  Summary: Diabetic nephropathy (DN), a microvascular complication of diabetes mellitus (DM), is the main cause of end stage **kidney disease** worldwide. There is a great need to find animal models of DM and DN that better resemble the physiopathological changes in humans. Both DM and DN are influenced by environmental factors and heredity. The SFBR has approximately 2400 baboons in a pedigreed colony, with a 10 cM linkage map available for 800 of these animals, and additional animals are being currently genotyped. Some baboons in this colony have developed clinical features of type-2 DM and 4 animals biopsied thus far have histological features similar to those found in humans with DN. Preliminary fasting blood glucose (FBG) screening of 478 baboons showed 44% with FBG equal to or > 126 mg/dl. Preliminary screening for microalbuminuria (MA) in 298 animals showed 33.5% of 149 control and 42% of 149 diabetic baboons had MA. One of the control and 3 of the diabetic baboons had proteinuria. A subset of 7 age- and weight- matched female baboons averaging 20 years of age underwent kidney biopsy, 4 diabetics and 3 controls. Diabetic animals had FBG > 126 mg/dl, hemoglobin A1C > 6%, abnormal intravenous glucose tolerance test and normal C-peptide levels. Kidney histology showed that diabetic animals had larger glomeruli, thickened glomerular basement membrane, mesangial matrix expansion and areas of mesangiolysis with early nodule formation. These histological changes closely resemble those of DN in humans, making the type-2 diabetic baboon a useful model of DN. We hypothesize that the characterization of the DN phenotype in genotyped baboons from the pedigree, confirmed by kidney biopsy, will allow us to run a genome-wide linkage analysis to identify genes and chromosomal regions associated with the development and progression of DN. We will conduct a population-wide screening in 1000 animals to study the prevalence of DM and the pattern of microalbuminuria in the baboon. The intrarenal renin-angiotensin system (RAS) is activated in DN, as evidenced by the heightened hemodynamic response to blockade of the RAS in human DN. We will characterize the phenotype of DN in a subset of animals and investigate the kidney expression of components of the RAS and other cytokines and matrix proteins associated with DN. We will then perform a genome-wide search to find and localize quantitative trait loci that influence variation in albuminuria and disease progression. Our goal is to identify early markers of disease progression amenable to intervention.

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

- **Project Title: PILOT/FEASIBILITY PROGRAM**

  Principal Investigator & Institution: Fogo, Agnes B.; 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: Visceral glomerular epithelial cells (podocytes) are a component of the glomerular filtration barrier. Due to a lack of ability for post-natal proliferation, the podocyte is a most vulnerable component of the glomerulus, and podocyte injury triggers irreversible change sin many glomerular diseases. The ultimate goal of this project is to elucidate the molecular mechanisms of podocyte damage through the study of the pathogenesis of HIV-1 associated nephropathy (IVAN). In HIVAN, glomeruli show a characteristic change, i.e., collapsing focal segmental glomerulosclerosis (FSGS), in which podocytes lose differentiation markers, proliferative and undergo apoptosis. Similar podocyte dysregulation is observed in idiopathic collapsing glomerulopathy and the FSGS variant with cellular lesion. In addition, down-regulation of differentiation markers occurs also in more common glomerular diseases, including minimal change disease and mesangial proliferative glomerulonephritis. Previous transgenic mouse studies showed than when HIV-1 DNA containing vif, vpr, rev and tat is expressed by the authentic LTR promoter, the kidney develops a renal disease faithfully mimicking human HIVAN. Renal cross transplantation between the transgenic and wild-type mice revealed that the transgene expressed in the kidney causes the renal disease. Based on this information, the following specific aims will be investigated during the first two years. Aim #1. Generation of transgenic mice in which podocyte-specific expression of HIV-1 gene that is essential for the pathogenesis of HIVAN by transgenic mice. These studies will be followed by identification of the specific molecule(s) in podocytes that are associated with the product of the pathogenic HIV-1 gene to ascertain the common mechanism(s) of podocyte dysregulation. Genetic studies of inherited polycystic **kidney disease** (PKD) in human and animal models have clearly shown that mutations at multiple loci result in various forms of PKD. While the cystogenesis itself is thought to be a primary cause of renal injury, several studies have stressed the important relationship between the onset of tubulointerstitial fibrosis, and the progression to end-stage renal disease. The PI has characterized a mouse model for PKD caused by three independent mutations, kat, kat21, kjat3J, that map to the same locus on Chromosome 8. By positional cloning, she has identified the gene mutated as the NIMA (Never In Mitosis A) related kinase, Nek1. The PI hypothesizes that in the kidney, NEK1 protein belongs to a signaling pathway that promotes the full maturation in renal tubular epithelial cells. The PI has also shown that the loss of Nek1 function leads to an increase in TGFbeta1 mRNA levels in renal interstitial as well as tubular cells. Therefore, these altered/immature renal epithelial cells may not only facilitate renal cystogenesis but also contribute directly to tubulointerstitial fibrosis. The PI is currently examining in her funded RO1 how the loss of Nek1 function leads to renal cystogenesis. In this pilot proposal she will pursue a new area of research: investigating the role of Nek1-null tubular epithelial cells in interstitial fibrosis. The hypotheses to be tested are: 1. The loss of Nek1 expression in renal tubular cells increases the activation of TGFbeta1 in those cells 2. The loss of Nek1 expression in renal tubular cells increases epithelial-mesenchymal transdifferentiation.

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

- **Project Title: PILOT--USING ZEBRAFISH MODEL OF PRONEPHROS DEVELOPMENT**

  Principal Investigator & Institution: Marrs, James A.; Associate Professor; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, in 462025167

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

  Summary: In this pilot project, zebrafish will be exploited to develop a model system to study kidney development. We propose a candidate gene approach to examine genetic control of pronephros development. Previous studies showed that histological features of metanephric kidney development in mammals are similar to the simpler pronephros development in fishes. In addition, critical gene expression patterns and developmental genetic pathways that control metanephric kidney development are also found in zebrafish pronephros development, showing that zebrafish pronephros is a powerful tool that complements studies of metanephric kidney development in mammals. Morpholino antisense oligonucleotides analogs suppress translation of specific genes, and morpholino oligonucleotide (MO) injection into 1-16 cell stage zebrafish embryos effectively produces a knockout for protein expression (termed MO knockdown) throughout the entire embryo for up to 50 hours postfertilization (hpf). Zebrafish development is very rapid, and a functional pronephros is produced by 48 hpf. Therefore, MO knockdown will allow us to examine specific gene function during renal tubule development. Using this approach, we can develop a zebrafish reverse genetic model for kidney tubule morphogenesis and genetic kidney disorders (for example, polycystic kidney disease). In this proposal, experiments are outlined that will determine the structural and functional consequences of (a) inhibiting expression of cadherin cell adhesion molecules that are expressed during pronephros development, (b) inhibiting expression of molecules that result in cystic disease in mammals (for example, inversion and Tg737), and (c) inhibiting expression of proteins that are found in developing and differentiated podocytes (for example, podocalyxin).

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

- **Project Title: POLYCYSTIC KIDNEY DISEASE AND MOUSE JCPK/BPK LOCUS**

  Principal Investigator & Institution: Flaherty, Lorraine A.; Director; Wadsworth Center Empire State Plaza Albany, Ny 12237

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

  Summary: (Adapted from the Applicant's Abstract): A new autosomal recessive mutation jcpk (juvenile congenital polycystic disease) was generated by chlorambucil mutagenesis. In the homozygous condition, this mutation causes a severe polycystic disease (PKD) which is more severe than previously described mouse PKD mutants. Homozygotes are detectable as early as 4 days and have grossly enlarged kidneys. Histologically, homozygote kidneys are highly abnormal even at birth, with cysts appearing throughout the kidney. Extreme dilatations of the bile ducts and pancreatic ducts are often seen. A late onset glomerulocystic disease is present in approximately 25% of the heterozygotes. The investigators have mapped the jcpk mutation to mouse chromosome 10. jcpk has recently been found to be allelic the bck mutation. By an extensive backcross, a fine genetic map of the region around the jcpk locus has been made. This map should enable the investigators to positionally clone the jcpk locus. The Specific Aims of the proposal are to: (1) build a YAC and BAC contig of the region surrounding the jcpk locus; (2) identify candidate genes for this locus; (3) identify, clone, and characterize the jcpk gene; and (4) characterize the genetics of cystic disease in +/jcpk heterozygotes. Arrayed cDNA libraries will be used for some of these studies. In

addition, genetic experiments involving DNA mismatch repair-deficient mice and transgenic mice will be conducted.

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- **Project Title: POLYCYSTIC KIDNEY DISEASE CLINICAL TRIALS NETWORK**

  Principal Investigator & Institution: Perrone, Ronald D.; Associate Professor; New England Medical Center Hospitals 750 Washington St Boston, Ma 021111533

  Timing: Fiscal Year 2002; Project Start 15-AUG-2002; Project End 31-JAN-2009

  Summary: (provided by applicant): Autosomal dominant polycystic **kidney disease** (ADPKD) is the most common lethal monogenetic disease, affecting 1/500 to 1/1000 of the US population. 50% of those affected with ADPKD will develop end-stage renal disease by the 6th decade of life. There are no proven therapies to slow the inexorable loss of kidney function in those with progressive disease. Interruption of the renin-angiotensin-aldosterone system (RAAS) has been shown to reduce the progressive decline in renal function in both diabetic and non-diabetic kidney diseases, but it is unknown whether these results extend to ADPKD. Abundant evidence implicates angiotensin II in the pathogenesis of hypertension, but small single-center studies of limited duration have reported inconsistent results of ACE inhibitor (ACE-I) therapy on disease progression. This application is submitted in response to RFA DK-01-029 to establish a PKD Clinical Trials Network of clinical centers that will each enroll 500 ADPKD patients and conduct a clinical trial to assess the efficacy of therapeutic interruption of the RAAS on renal progression. We have proposed a randomized, double-blinded trial to compare ACE-I vs. active control in hypertensive ADPKD patients with renal insufficiency (GFR 30-65 ml/min/1.73 m2) on the time to reach a composite outcome of doubling of serum creatinine, ESRD, or death. The Clinical Center will be based at the New England Medical Center and Beth Israel Deaconess Medical Center. The Principal and Co-Principal Investigators have had career-long interests in ADPKD and personally care for large numbers of ADPKD patients. We have identified 107 potentially eligible patients within our clinical sites. Additional strategies will be used to target patients locally and within contiguous New England States. Strong institutional support is available at the highest levels, including the General Clinical Research Centers at NEMC and BIDMC. As part of this RFA, we have proposed a pilot study to assess the safety of cyclooxygenase-2 inhibition, which has been implicated in angiogenesis and cyst development in animal models of ADPKD. Thirty ADPKD patients with GFR >70 ml/min/1.73 m2 will be randomized to treatment with celecoxib vs. placebo and followed for 16 weeks. Change in GFR is the primary outcome measure and incidence of hyperkalemia, fluid retention, and elevated blood pressure will be assessed.

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- **Project Title: POLYCYSTIN-1 INTERACTION WITH TSC-2 IN POLYCYSTIC KIDNEY DISEASE**

  Principal Investigator & Institution: Guan, Kun-Liang; Associate Professor; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

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

  Summary: Autosomal dominant polycystic **kidney disease** (ADPKD) is one of the most common genetic disorders in humans. In the United States, ADPKD is more common than cystic fibrosis, Huntington's disease, and muscular dystrophy. ADPKD is characterized by the formation of cysts in kidney and caused by mutation in either

PKD1 (85%) or PKD2 (15%) gene. Tuberous sclerosis (TSC) is an autosomal dominant inheritable genetic disorder due to mutation in either TSC1 or TSC2 gene. TSC is characterized by formation of hamartomas in various tissues. Cyst formation in kidney is also observed in TSC. The PKD1 and TSC2 genes are located adjacent to each other on human chromosome 16p and deletion of both genes results in a contiguous gene syndrome responsible for the severe infantile polycystic **kidney disease.** TSC2 has been implicated to play a role in the proper functions of polycystin-1, the product of PKD1 gene. The long-term goals of this project are to understand the functional relationship between TSC2 and PKD1 and to elucidate the molecular mechanism of TSC2 in regulation of PKD1 function and ADPKD. The specific aims of this proposal are to elucidate the mechanism of TSC2 regulation by osmotic stress and to investigate the function of TSC2 in regulation of the plasma membrane localization of polycystin-1.

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- **Project Title: PREVENT/KIDNEY DISEASE/MINORITY GROUPS/EMERGING NATIONS**

  Principal Investigator & Institution: Norris, Keith C.; Professor; None; Charles R. Drew University of Med & Sci 1621 E 120Th St Los Angeles, Ca 90059

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-AUG-2004

  Summary: (provided by applicant): Charles R. Drew University of Medicine and Science (Drew) proposes to co-sponsor a satellite conference to the annual American Society of Nephrology (ASN) "Renal Week" meetings for the next five years. The meetings will focus on chronic **kidney disease** (CKD) and cardiovascular complications in ethnic and disadvantaged groups with carefully selected speakers, presenting junior investigators, and organizing committee members from multiple countries, focusing on Central and South America. Main topics will include prevalence of CKD, its main causes, early detection, prevention and access to renal replacement therapy. The title for this year's planned symposium is "Prevention of **kidney disease** in minority groups and emerging nations." This symposium stems from the growing global problem of progressive renal disease among racial and ethnic minorities. The proceedings of a similar 2001 symposium, which was an official satellite conference to the annual American Society of Nephrology meeting, was the subject of a recent Kidney International journal supplement that comprised of 28 articles (Volume 63, 2003). The overarching goal is to develop a symposium where kidney specialists discuss the burgeoning problems that beset racial and ethnic minority groups worldwide as related to progressive renal disease. The symposium will allow for the presentation and discussion of epidemiological, clinical, and basic science advances by a diverse international panel. The Drew Prevention of **Kidney Disease** in Racial and Ethnic Minority Groups Symposium application has four Specific Aims: Specific Aim 1: To organize and implement symposiums focusing on the prevention of **kidney disease** in minority groups and emerging nations as a satellite to the American Society of Nephrology annual meeting; Specific Aim 2: To increase knowledge and therefore, increase prevention of chronic **kidney disease** in minority groups and emerging nations; Specific Aim 3: To cultivate junior investigators' involvement in studies regarding the relationship between **kidney disease** and minority groups/emerging nations; and Specific Aim 4: To develop and publish a supplement that comprises of articles from each of the speakers at the symposium for the Kidney International Journal.

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

- **Project Title: REGULATION OF ENDOCYTIC TRAFFIC IN KIDNEY CELLS**

  Principal Investigator & Institution: Apodaca, Gerard L.; Associate Professor of Medicine; Medicine; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2001; Project Start 01-DEC-1996; Project End 30-NOV-2001

  Summary: The generation of distinct apical and basolateral plasma membrane domains is vital to the function of polarized kidney epithelia. In response to ischemia, or as a result of hereditary disease (e.g. polycystic **kidney disease** or microvillus kidney disease), kidney cells loose their polarity and as a result there is a loss of cellular function and ultimately kidney dysfunction. The cell surface polarity of these cells is achieved by several mechanisms including direct delivery of proteins from the trans-Golgi network, and specialized endocytic pathways that allow endocytosis of plasma membrane proteins/lipids and their subsequent return to the plasma membrane (recycling), selective degradation in lysosomes, or delivery to the opposite plasma membrane domain (transcytosis). Transcytosis is central to the establishment of kidney cell polarity, as it is the only pathway for delivery of newly synthesized membrane proteins to the apical cell surface that is universally found in all epithelial cells examined. Recycling is crucial because it allows these cells to maintain their polarized distribution of proteins and lipids by retrieving both membrane and proteins between adjacent compartments of the endocytotic and biosynthetic pathways. Epithelial cells are known to have distinct populations of apical and basolateral early endosomes, which when labeled with fluid phase markers do not exchange contents. However, it is now known that membrane proteins can transit between basolateral endosomes and a specialized apical endosomal compartment called the apical recycling endosome (ARE). This tubular/vesicular compartment contains not only transcytosing molecules, but recycling ones as well, and is characterized by its accessibility to membrane markers, but inaccessibility to fluid-phase ones. It is hypothesized that this compartment may be a major sorting organelle in polarized epithelia, and may also be the principal site for regulating protein traffic to the apical pole of these cells. The aims of this proposal are to: i. determine if sorting of transcytotic and recycling proteins occurs in the ARE, ii. examine the regulation of proteins recycling basolaterally, and that of proteins recycling and transcytosing from the ARE, and iii. purify the ARE compartment in order to identify other cargo molecules, and proteins that may regulate its function.

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- **Project Title: REGULATION OF EXTRACELLULAR MATRIX IN KIDNEY DISEASE**

  Principal Investigator & Institution: Border, Wayne A.; Professor; Internal Medicine; University of Utah 200 S University St Salt Lake City, Ut 84112

  Timing: Fiscal Year 2001; Project Start 30-SEP-1990; Project End 30-AUG-2004

  Summary: The cytokine transforming growth factor-beta (TGF-beta) is a key biological mediator of extracellular matrix deposition in health and in fibrotic diseases, especially of the kidney. We have demonstrated a central role for TGF-beta in the pathogenesis of experimental and/or human forms of acute and chronic glomerulonephritis, diabetic nephropathy, hypertensive nephropathy, acute and chronic allograft rejection, cyclosporine nephropathy and HIV-associated nephropathy. TGF-beta is also implicated in numerous fibrotic disorders involving other tissues and organs and is considered to be a principal target for designing novel therapeutic agents to block fibrotic disease. An important question is what is the cause of the persistent TGF-beta overexpression that leads to progressive fibrosis and kidney failure? In the course of our work we have

discovered a complex interconnection between TGF-beta and the renin-angiotensin system (RAS) in the kidney. The RAS acts to stimulate the production and activation of TGF-beta and to increase the expression of TGF-beta receptors which greatly enhances TGF-beta's fibrotic effects. We hypothesize that continued stimulation of TGF-beta by the RAS may be a molecular mechanism for the continued overexpression of TGF-beta in kidney diseases. In this application we propose to investigate the molecular interconnections by which the RAS may perpetuate the actions of TGF-beta and to explore in vivo therapeutic strategies to block these effects by doing the following: 1) Investigate a molecular mechanism by which angiotensin II may up-regulate TGF-beta receptors by analyzing the functional elements of the TGF-beta type I receptor promoter in the kidney, 2) Investigate the possibility that renin or prorenin may be up-stream effectors that, especially in the presence of angiotensin II blockade, induce TGF-beta overexpression and thus contribute to progressive fibrotic disease and 3) Continue investigation of the role of interactions between the renin-angiotensin system, TGF-beta overexpression and TGF-beta receptor expression in the pathogenesis of fibrosis using a model of acute glomerulonephritis and to compare the findings with parallel studies in a model of chronic glomerulonephritis. The significance of this application is that it will apply new knowledge and technology to an area of investigation that is directly relevant to improved understanding of the pathogenesis of kidney fibrosis and will likely provide insights that suggest new therapeutic strategies to prevent progressive kidney failure in humans suffering from **kidney disease.**

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- **Project Title: REGULATION OF GROWTH AND EPITHELIAL TRANSPORT IN ADPKD**

  Principal Investigator & Institution: Fitz, Gregory; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

  Timing: Fiscal Year 2001; Project Start 01-APR-1985; Project End 30-JUN-2006

  Summary: Hepatic cysts represents the most common extrarenal manifestation of autosomal dominant polycystic **kidney disease** (ADPKD), are associated with significant clinical morbidity, and account for up to 10% of mortality in affected patients. Despite the recent identification of genes responsible for ADPKD, little is known regarding the cellular mechanisms involved in the formation and maintenance of liver cysts; or the regulation of growth and secretion in cholangiocytes, the epithelial cells affected by hepatic ADPKD. Clinical studies support a potential role for estrogen in the progression of complicated hepatic cystic disease, and laboratory studies have implicated autocrine signaling by epidermal growth factor and purinergic agonists (e.g., ATP) as key contributors to aberrant cyst growth. However, there are no tissue culture models of ADPKD-affected cholangiocytes currently available. Recent studies by ourselves and ourselves have led to new approaches to isolation and long term culture of polarized cholangiocyte models; and to the application of biophysical and molecular techniques to address the cell-specific mechanisms that modulate biliary secretion, growth, and differentiation. The proposed studies will utilize these approaches to investigate the properties of cholangiocytes derived from the cysts of ADPKD animal models to address whether the development of liver cysts in ADPKD is associated with i) disordered growth and/or secretion across biliary- derived epithelial and ii) abnormalities of autocrine/paracrine signaling pathways. The Specific Aim focus on the development of novel rat and mouse ADPKD liver cyst epithelial cell models in order to characterize mechanisms that regulate growth, differentiation, and transport in normal versus ADPKD cholangiocytes. Emphasis will be placed on the regulatory pathways

that modulate ADPKD cholangiocyte secretion and differentiation by focusing on membrane transport and the potential roles of estrogen, growth factors, and purinergic signaling. The long-term goals of this project are to generate an understanding of the mechanisms that contribute to hepatic cyst pathogenesis, and to use these findings as a basis for development of pharmacological and other approaches aiming to attenuate cyst-associated morbidity in patients with ADPKD-related hepatic cysts.

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- **Project Title: RENAL TUBULOGENESIS AND THE ROLE OF HGF/SF AND SYNTAXINS**

  Principal Investigator & Institution: Lipschutz, Joshua H.; Medicine; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2001; Project Start 15-SEP-1997; Project End 30-JUN-2002

  Summary: Many vital organs, including the kidney, form as a result of a mesenchymal-epithelial interaction. A mediator of these interactions is hepatocyte growth factor, a. k. a. scatter factor, (HGF\SF). HGFISF is mesenchymally-derived growth factor and ligand for the epithelial c- rnet receptor. Though HGFISF is not the only inducer of renal development and tubulogenesis, it induces tubulogenesis both in vivo and in vitro ii Madin-Darby canine kidney (MDCK) cells, which are derived from canine renal tubular epithelium. Generation and maintenance of cell polarity is essential to epithelial cell function. To establish and maintain their polarity, epithelial, including MDCK, cells must send plasma membrane (PM) proteins to th(correct apical or basolateral PM. Preliminary results show that when HGF/SF induced tubulogenesis occurs MDCK cells lose their polarity as they branch out and then regain their polarity as the new tubules form. A major discovery in recent years is that almost all intracellular membrane traffic uses a common machinery for membrane fusion. Syntaxins are a gene family and component of the membrane fusion machinery that appear to specify correct delivery to the different PM surfaces. Syntaxins 2, 3, and 4 are abundant in epithelial organs, e.g. kidney. Syntaxins 2, 3, and 4 were found to be differentially expressed in MDCK cells, with syntaxins 3 and 4 having a completely non- overlapping distribution. Syntaxins are the first molecules that are part of the membrane fusion machinery, whose isoforms are differentially localized and whose overexpression has differential effects on polarized membrane traffic. Hence, they are the leading candidates for containing at least part of the information needed for the maintenance of cell polarity. The hypothesis is that transient loss of cell polarity i crucial for renal tubulogenesi: and syntaxins are involved in controlling cell poladty and therefore tubulogenesis. The expression and localization of syntaxins will be examined during HUF/SF induced tubulogenesis in MDCK cells, normal development of rodent kidneys, and abnormal development in disease states such a polycystic **kidney disease** and renal cell carcinoma. To directly test the hypothesis, the expression an function of different syntaxins will be perturbed by overexpression, inhibition of expression, and dominar negative mutants. If the expression of syntaxins is important for tubulogenesis, consideration can be given t finding ways to alter syntaxin expression in disease states, perhaps by gene therapy using viral vectors.

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- **Project Title: RESEARCH TRAINING IN RENAL DISEASE**

  Principal Investigator & Institution: Couser, William G.; Professor; Medicine; University of Washington Seattle, Wa 98195

Timing: Fiscal Year 2003; Project Start 15-JUL-1993; Project End 30-JUN-2008

Summary: (provided by applicant): This grant requests support to continue a research training program for physician-scientists committed to pursuing research into the causes and cures of **kidney disease. Kidney disease** affects over 13 million Americans. Almost 300,000 have end-stage renal disease, a figure which increases 7% each year and costs the federal government over 12 billion dollars annually for dialysis and transplantation support. This program will provide three years support for research training to three physicians each year selected by a selection committee. Trainees will be MDs/PhD's or PhD's from nephrology or other disciplines who are committed to pursuing a career in renal-related research and have the requisite skills to achieve this goal. Extensive efforts to recruit under-represented minorities will be made. The program will be directed by Dr. William Couser who has been the Program Director for the past 19 years. It will be co-directed by Dr. Stuart Shankland, an active basic investigator in nephrology. Seven physicians in nephrology will serve as primary mentors. All members of the nephrology program staff have productive, federal and non-federal-funded research programs studying renal diseases including acute and chronic immune glomerular diseases, diabetes, hypertension, and acute renal failure at a basic cellular and molecular level. Nephrology program staff will serve as primary mentors for trainees who will spend 1-2 years with these individuals before beginning a 1-2 year period of intensive training in basic science with one of the 14 members of the basic science program staff. All members of the basic science program staff have well-funded research programs in basic science with potential application to **kidney disease,** have established collaborative scientific interactions with members of the nephrology program staff, and have extensive experience in research fellowship training. Thus, individual research training programs will be tailored for each trainee based on his/her own area of interest and long-term goals. Didactic training will also be provided in cell and molecular biology and research integrity. The program is multi-disciplinary supporting trainees in several different departments and is overseen by an Advisory Committee of three prominent and experienced senior research mentors. Of 12 individuals supported during the first 10 years of this program, 5 currently hold academic positions, 4 have federally-funded research programs, 5 are still in training and 2 have entered into practice.

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- **Project Title: RESISTANCE TRAINING DURING MAINTENANCE DIALYSIS**

  Principal Investigator & Institution: Sceppa, Carmen C.; Nutrition Exercise Physiology Sarcopenla (Neps) Lab; Tufts University Boston Boston, Ma 02111

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

  Summary: (provided by applicant): There is a rising incidence of kidney failure in the US, with poor outcomes and high cost. End-stage renal disease (ESRD) affects almost 375,000 individuals in the US at a cost of more than $14 billion per year. Despite advances in dialysis and transplantation therapies, kidney failure leads to poor outcomes, poor prognosis and high health care costs. Malnutrition and the underlying systemic inflammatory response developed during the course of chronic **kidney disease,** worsen during ESRD, and leads to adverse outcomes, increased morbidity and mortality. Muscle wasting, impaired functional capacity and poor quality of life are the most important factors associated with malnutrition and inflammation in renal failure. We have shown in pre-dialysis patients with moderate chronic renal insufficiency that the anabolic effects of resistance exercise training result in significant improvements in protein utilization, nutritional status and functional capacity even in the context of

anorexia and prescribed low protein diets. Thus, we propose to develop, test and implement a progressive resistance exercise routine for ESRD patients during the hemodialysis session. Our hypotheses are that the addition of 30-45 min of resistance exercise training during the dialysis session will counteract the burden of renal disease and will result in: 1) A feasible and safe exercise modality for ESRD patients (6-wk feasibility phase tested in 10 patients); 2) Net anabolism as evidenced by: improved nutritional status (i.e. increased protein catabolic rate, muscle mass and muscle strength); and reduced systemic inflammatory response (i.e. reduced C-reactive protein and interleukin-6, and increased serum albumin levels) compared to a randomly assigned control group on hemodilaysis but not exercise training (6-mo efficacy phase tested in 20 patients/group); and that 3) Improved self-reported physical function (i.e. increased SF-36 physical component scale) observed with resistance training will be associated with the improvements in nutritional status and inflammatory response. The long-term goal is to implement resistance exercise training routines during hemodialysis to overcome the underlying malnutrition and inflammation of ESRD and to improve disease outcome and prognosis. By implementing such intervention, we hope to offer a therapeutic strategy that can be incorporated to the standard of care of ESRD patients by working in conjunction with the dialysis unit staff.

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- **Project Title: ROLE OF KAP EXPRESSION IN THE DIABETIC KIDNEY**

  Principal Investigator & Institution: Coschigano, Karen T.; None; Ohio University Athens Athens, Oh 45701

  Timing: Fiscal Year 2002; Project Start 01-JUL-2002; Project End 30-JUN-2004

  Summary: (provided by applicant): Kidney damage is a frequent complication of both type I and type II diabetes, often ending in kidney failure, or end-stage renal disease (ESRD). Diabetic nephropathy, the single most common cause of ESRD, is a progressive disease that takes several years to develop and often goes undiagnosed. The long-term goal of this project is to design specific, targeted markers and therapeutic approaches for the diagnosis, treatment, and prevention of human diabetic **kidney disease.** Toward this end, previous work identified a cDNA whose mRNA expression decreases markedly with increasing kidney damage, both in a diabetes-dependent and in a diabetes-independent mouse model of glomeruloscierosis. This cDNA encodes kidney androgen-regulated protein (KAP), a kidney-specific protein found only in renal proximal tubule cells. Since decreasing levels of KAP mRNA are associated with progressive kidney damage, it is proposed that maintenance of high levels of KAP mRNA expression will protect the kidney from glomerular hypertrophy and diabetic damage. This hypothesis will be tested by expressing KAP mRNA in the kidneys of mice under the direction of a heterologous promoter and then assessing the extent of kidney damage after induction of diabetes by streptozotocin injection. Acceptance of the hypothesis could lead to the development of KAP as a therapeutic drug for the prevention of kidney damage.

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- **Project Title: SPECIFICATION OF THE AVIAN INTERMEDIATE MESODERM**

  Principal Investigator & Institution: Schultheiss, Thomas M.; Assistant Professor; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

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

  Summary: (provided by applicant): All vertebrate kidney tissue is derived from the intermediate mesoderm (IM), a strip of tissue that lies between the somites and the

lateral plate in the developing embiyo. Although much progress has been made in understanding later stages of kidney development, during which the IM differentiates into kidney tubules, very little is known about the critical, early stages in which the IM itself is generated. The proposed studies investigate the embryological mechanisms which regulate IM formation in the avian embryo. The avian embryo is used because it can be experimentally manipulated throughout the process of IM formation, allowing a broad range of in vivo and in vitro studies to be performed. In the first part of the proposal, a range of in vivo and in vivo experimental manipulations will be performed to identify the embryonic tissues that are the sources of signals that pattern the IM. In the second part, the role in IM specification of one such signal, Retinoic Acid (RA), will be investigated. A line of Vitamin A deficient (VAD) quails, which are deficient in RA signaling, will be used to determine the dependence of IM development on RA signaling. The effects of ectopically applied RA and RA antagonists on IM gene expression will also be studied. Finally, the role of Hox genes, a potential target of RA signaling, in regulating the formation of the anterior border of the IM will be investigated using targeted gene misexpression via an avian retrovirus. **Kidney disease** is a leading cause of morbidity and mortality in the United States. One potential treatment approach to **kidney disease** is to supplement kidney function with grafts of kidney tissue that have been generated in the laboratory. Efforts to generate kidney tissue in vitro would be greatly facilitated by knowledge of how kidney tissue is generated in vivo, in the developing embryo. The current experiments directly tackle this problem by attempting to uncover the signaling events that regulate IM formation. The experiments with RA (Aim 2) should be directly relevant to efforts to generate IM in vitro, while the experiments of the first part of the proposal will lay the groundwork for future experiments aimed at identifying other molecular mediators of IM formation. In addition, congenital defects of the nephric system are one of the most common types of birth defects in humans, and Vitamin A deficiency is a known cause of congenital **kidney disease.** The experiments in the second part of this proposal may shed light on the embryological mechanisms underlying a portion of the cases of congenital nephric system malformations.

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- **Project Title: THE AASK COHORT STUDY**

  Principal Investigator & Institution: Cleveland, William H.; Medicine; Morehouse School of Medicine Atlanta, Ga 30310

  Timing: Fiscal Year 2003; Project Start 29-SEP-2003; Project End 30-JUN-2007

  Summary: (provided by applicant): Hypertensive **kidney disease** commonly progresses. The primary objective of the AASK (African American Study of **Kidney Disease** and Hypertension) Cohort Study is to determine prospectively the course of kidney function and risk factors for **kidney disease** progression in African-Americans with hypertensive **kidney disease** who receive recommended antihypertensive therapy. A secondary objective is to determine the occurrence of cardiovascular disease and assess its risk factors. The AASK Cohort Study is a prospective, observational study that is an extension of the AASK trial. The AASK trial tested the effects of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol and amlodipine) and 2 levels of blood pressure control. Of the 1,094 trial participants, approximately 650 to 700 individuals who have not reached end stage renal disease (ESRD) will likely enroll in the Cohort Study. Risk factors to be studied include environmental, genetic, physiologic, and socio-economic variables. The primary renal outcome is a composite clinical outcome defined by doubling of serum creatinine, ESRD, or death. Medication

treatment for hypertension, beginning with the angiotensin converting enzyme inhibitor ramipril, is offered to all participants. In this fashion, the study directly controls two of the major determinants of **kidney disease** progression (treatment of hypertension and use of reno-protective, antihypertensive medication). The minimum duration of follow-up in the Cohort Study is 5 years (total of 9 to 12 years, including the period of the AASK trial). Ultimately, data from the AASK Cohort Study should enhance our understanding of the risk factors and processes that determine the progression of **kidney disease.** Such results might eventually lead to new strategies that delay or prevent ESRD.

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- **Project Title: THE PROTEOLYTIC CLEAVAGE OF POLYCYSTIN-1: HOW AND WHY**

  Principal Investigator & Institution: Qian, Feng; Assistant Professor of Medicine; Medicine; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

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

  Summary: (provided by applicant): Autosomal dominant polycystic **kidney disease** (ADPKD) is one of the most common Mendelian disorders in humans affecting 1/1000 worldwide. The hallmark of the disease is the development of multiple cysts from renal tubules in both kidneys, resulting in end-stage renal failure in 50% of the patients. ADPKD is a systemic disease with many ex-renal manifestations. Since the PKD1 gene was identified in 1995, significant efforts have been made in understanding of the biology underlying the disease. But the normal function its gene product, polycystin-1, is still poorly understood. The question of how a mutation in the single PKD1 gene leads to a vast array of defects is also unresolved. The long-term goal of our research is to understand the normal biological function of polycystin-1 during the development and its role in the maintenance of adult organs, and the mechanisms by which PKD1 mutations cause the disease. Post-translational modifications of the protein are known to play a critical role for its activity and such processes have been implicated for the function of polycystin-1. We have found that polycystin-1 undergoes proteolyctic cleavage in vivo. Our preliminary results have indicated that this type of the post-translational processes is likely important for the functionality of polycystin-1. In the grant application, we propose to investigate the role of the proteolytic cleavage of polycystin-1 using a combination of chemical, biochemical, genetic and cell biological approaches. We plan to examine the functional significance of this process in the cell culture system and in the mouse. Furthermore, we propose to characterize the mechanism of regulation of the cleavage reaction and analyze the cellular machinery of the process. This scientific query will likely provide important insights into the functions and novel mechanism of the regulation of potycystin-1. Our investigation will also likely provide clues of the mechanisms by which PKD1 mutations cause the disease. The information from our studies will likely open new avenues in the research of ADPKD and establish the foundation for developing causative and effective therapies of the disease.

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

- **Project Title: THE ROLE OF BMP-7 IN CHRONIC KIDNEY DISEASE**

  Principal Investigator & Institution: Hruska, Keith A.; Professor of Pediatrics; Pediatrics; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2002; Project Start 24-APR-2002; Project End 31-MAR-2006

Summary: Bone morphogenetic protein-7, BMP-7, is a critical renal morphogen that is required for development but continues to be expressed at high levels in adult renal tubular segments. Recent studies have demonstrated that BMP-7 prevents the tubulointerstitial nephritis associated with chronic renal injury. BMP-7 appears to function as a hormonal differentiation factor and one of its effects, as such, may be to suppress the transcription of genes activated by various renal injuries. This function would suggest strong therapeutic potential for such a hormone in its target tissues. The therapeutic targets of BMP-7 include the skeleton, the vasculature and the kidney. In the kidney, specific BMP-7 receptors are expressed in the collecting duct, proximal tubule and the glomerulus. The long-range objective of this application is to analyze the efficacy of BMP-7 in various forms of chronic **kidney disease** (CKD). The studies in the application will address two hypotheses. The first is that BMP-7 is an effective therapeutic agent in CKD. Since many forms of CKD are accompanied by a major tubulointerstitial component in their later stages, we propose that the usefulness of BMP-7 will be more general than disease specific. A second hypothesis to be tested is that replacement of BMP-7 in chronic kidney failure will maintain bone remodeling rates in the absence of secondary hyperparathyroidism. Recent data suggest that CKD is associated with a reduction in the osteoblast differentiation program such that in the absence of secondary hyperparathyroidism an adynamic bone disorder is observed. Studies in the application will demonstrate that BMP deficiency is a likely cause of the reduction in osteoblast differentiation produced by CKD. The specific aims of the application are to analyze the therapeutic effectiveness of BMP-7 in animal models of CKD; to analyze the effect of BMP-7 in the treatment of renal osteodystrophy; and to analyze the mechanism of action of BMP-7 in inhibiting renal fibrogenesis. Protocols are proposed to demonstrate the therapeutic effectiveness of BMP-7 in the streptozotocin rat model of diabetic nephropathy and of cyclosporine-induced arteriolopathy and nephrosclerosis. A murine 5/6 nephrectomy model will be used to test the effectiveness of BMP-7 in restoring osteoblast differentiation in CKD associated with suppression of secondary hyperparathyroidism. Successful completion of the proposed studies will significantly clarify the usefulness of BMP-7 in CKD, and encourage its development as a new therapeutic agent.

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

- **Project Title: THE ROLE OF POLYOMAVIRUSES IN PEDIATRIC RENAL DISEASES**

  Principal Investigator & Institution: Vanchiere, John A.; Pediatrics; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2002; Project Start 21-AUG-2002; Project End 31-JUL-2007

  Summary: (provided by applicant): As a pediatric infectious disease fellow, I have been impressed with problems due to chronic virus infections in immune-compromised children. My long-range goal is to understand host and viral factors responsible for viral persistence. Human polyomaviruses, JCV and BKV, are nephrotropic viruses acquired early in life that persist asymptommatically in immune competent hosts. SV40 is a polyomavirus of macaque origin that was introduced into the human population as a contaminant of early polio vaccines and has been linked to several human cancers. Recent studies from our laboratory have found an association between SV40 and renal disease in children, especially post-transplant. Based on human and animal studies, others have linked SV40 to focal segmental glomerulosclerosis (FSGS), an enigmatic **kidney disease** that is increasing in incidence in both children and adults. Children with FSGS are a subset of children with nephrotic syndrome (NS) who fail to respond to

steroid therapy and generally progress to end-stage renal disease, necessitating kidney transplantation; FSGS frequently recurs in the new kidney. Our working hypothesis is that SV40 and/or the immune response to SV40 play a role in the pathogenesis of NS and FSGS in children. The experimental approach will also reveal if JCV or BKV play a role in these diseases. Prospective studies of children with NS and various forms of immune suppression will test this hypothesis. Polyomavirus (SV40, JCV and BKV) infection and excretion in these groups and in children from the general pediatric population will be evaluated by PCR and sequence analysis, culminating with an analysis of strain variation to determine whether some viral strains may be more pathogenic than others. Cell-mediated immune responses are vital to the ability of the host to control polyomaviruses. To test the hypothesis that an unbalanced SV40 immune response plays a role in renal disease, SV40-specific antibody titers will be determined by plaque neutralization and SV40-specific cellular immune responses in children will be characterized using a conventional assay of interferon production and, when possible, an HLA-peptide tetramer assay that can identify SV40-specific cytotoxic T lymphocytes. These studies will have implications for the treatment and prevention not only of renal diseases but also for SV40-related malignancies and polyomavirus-related diseases in post-transplant patients and individuals with HIV and AIDS. They also will provide me a firm foundation on which to build an academic career. Dr. Butel's laboratory provides an excellent environment in which to develop my scientific skills.

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

- **Project Title: THE ROLE OF TGF-ALPHA IN THE PATHOGENESIS OF ARPKD**

  Principal Investigator & Institution: Dell, Katherine M.; Pediatrics; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

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

  Summary: (adapted from the application) Autosomal recessive polycystic **kidney disease** (ARPKD) is an inherited kidney disorder characterized by massive kidney enlargement and hepatic fibrosis. Progression to end-stage renal disease is usually inevitable, often in the first years of life. A growing body of literature has established a key role for the epidermal growth factor receptor (EGFR) in the pathogenesis of abnormal cell proliferation and cyst expansion. In contrast, the expression, regulation, and function of the EGFR ligands have not been studied systematically in these diseases. Published data demonstrate that the EGFR ligand, transforming growth factor-alpha (TGF-alpha), is overexpressed in cystic tissues and cells and transgenic mice that overexpress TGF-alpha develop renal cysts. Using TGF-alpha as a paradigm, the proposed research will examine the physiologic effects of ligand upregulation and identify factors that contribute to EGFR ligand overexpression in ARPKD. The central hypothesis is that aberrant EGFR ligand expression is a common feature modulating the cellular pathophysiology of PKD. The specific aims of the project are: 1. To examine the physiologic effects of TGF-alpha upregulation in cyst formation and enlargement and to identify specific factors mediating TGF-alpha upregulation. Specific hypothesis to be tested include: a) TGF-alpha upregulation results in increased production of itself (auto-induction) and other EGFR ligands (cross-induction); b) secreted, not membrane-bound TGF-alpha, is the more important biologically-active moiety in ARPKD; c) TGF-alpha regulates EGFR expression by direct effects on EGFR mRNA transcription and stability; and d) abnormal expression of AP-2 and VHL, factors known to regulate TGF-alpha expression, mediate increased TGF-alpha expression in ARPKD. Primary and immortalized collecting tubule (CT) cell lines derived from cystic bpk mice (a murine model of ARPKD) and noncystic littermates will be used to assess the in vitro effects of

exogenous TGF-alpha administration, TGF-alpha overexpression, and TGF-alpha/EGFR interactions. AP-2 and VHL protein and mRNA expression in cystic and control tissues and cells will be determined, and the role of each protein in TGF-alpha regulation assessed. 2. To determine the in vivo effects of blocking TGF-alpha production on disease progression in ARPKD. The hypothesis to be tested is that TGF-alpha has a key role in the pathogenesis of ARPKD. This will be tested by breeding the bpk mouse with a TGF-alpha knockout mouse and assessing the impact on disease progression and expression of EGFR and other EGFR ligands. These studies will provide new insights into the biology of EGFR ligands in ARPKD. Although the proposed research focuses on ARPKD, insights provided by these studies may contribute to a broader understanding of autosomal dominant polycystic **kidney disease** (ADPKD) as well.

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

- **Project Title: TYPE IV COLLAGEN IN ALPORT SYNDROME PATHOGENESIS**

  Principal Investigator & Institution: Kalluri, Raghu; Associate Professor; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

  Timing: Fiscal Year 2001; Project Start 15-AUG-1999; Project End 31-JUL-2003

  Summary: Alport syndrome is a common disorder that results in progressive **kidney disease,** and is occasionally associated with hearing loss and eye defects. The most common form of Alport syndrome is inherited as an X-linked trait (XAS), and is due to mutations in the alpha5 chain, one of six genetically distinct isoforms of type IV collagen. Rare autosomal recessive forms of the disease also exist, and are due to mutations in the alpha3 or alpha4 chains of type IV collagen. Type IV collagen is a major component of the glomerular basement membrane (GBM) and is predominantly composed of alpha3, alpha4 and alpha5 isoforms of type IV collagen. Mutations in any one of these isoforms in Alport syndrome leads to an absence of all three isoforms from the GBM of these patients, making their membranes more susceptible to breakdown by proteases. These results suggest a molecular association between the three isoforms in the kidney GBM. In the first part of this proposal we plan to study the relationship between the structure of GBM type IV collagen and the turnover of this membrane in Alport syndrome, using human Alport kidneys and kidneys from mice with Alport-like disease. These studies will determine the structural organization of type IV collagen in the human GBM and how such organized networks are altered by mutations in Alport syndrome. In the second part of this proposal, we will identify specific populations of NC1 hexamer in the human GBM and how mutations in Alport syndrome effect their assembly. We will use recombinant NC1 domains of alpha3, alpha4 and alpha5 chains produced in NIH 3T3 cells for in vitro hexamer assembly experiments. The role of mutated alpha3 chain in the in vivo assembly of GBM type IV collagen will be evaluated in transgenic mice. Lastly, the role of alpha5 chain (X-linked Alport gene) will be studied in mice, made deficient for this gene by gene targeting technology. These mice will be valuable in understanding the molecular events leading to defects in the Alport GBM due to mutations in the alpha5 chain. Successful completion of this project will determine the role of type IV collagen in the GBM turnover and identify molecular parameters for the assembly of type IV collagen NC1 hexamer which turns defective in Alport syndrome. A consideration of the differential sensitivity of GBM in XAS to degradation might perhaps at some point lead to therapeutic trials with new generation protease inhibitors now emerging for clinical use.

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

- **Project Title: TYROSINE KINASES AND B LYMPHOCYTE TOLERANCE**

  Principal Investigator & Institution: Defranco, Anthony L.; Professor; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

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

  Summary: The immune system must decide whether to mount an immune response to a particular entity or whether to ignore the latter outcome as referred to as immunological tolerance. A great deal has been learned about tolerance over the past decade, but our understanding is still fragmentary, despite its importance for understanding autoimmune disease, managing acceptance of organ transplants, promoting cancer immunotherapy, and decreasing the complication of allosensitization by transfusion of platelets and other blood products. In the previous project period, we unexpectantly found that mice deficient in the Lyn tyrosine kinase have B lymphocytes that exhibit elevated responsiveness to antigenic stimulation. In vivo, these mice make high levels of autoantibodies directed at nuclear components such as double-stranded DNA and some of them develop **kidney disease.** Double mutant mice defective in Lyn and another Src-family kinase, Fyn were found to develop a much more severe autoimmune lupus-like **kidney disease,** with 50% of the animals dying by 7 months of age. We hypothesize that the defect in lyn makes B cells hyperresponsiveness and also defective in tolerance induction, resulting in production of antibodies directed at nuclear components released by apoptotic cells. We further hypothesize that the defect in fyn contributes to more rapid disease, possibly by making the kidneys more susceptible to damage resulting from immune complex deposition. These hypotheses will be tested by four Specific Aims. 1) We shall define the cellular basis of defects leading to autoimmune diseases in lyn-/-,fyn-/- mice. This will be done by bone marrow transplantation and by adoptive transfer of mature lymphocytes. 2) We shall define the effects of the Fyn- deficiency on B cell phenotype, signaling ability, and activation, both in the context of otherwise normal mice and in the context of the Lyn- deficiency. We hypothesize that in contrast to Lyn, Fyn is a positive element in antigen receptor signaling, so its loss will decrease B cell responsiveness to antigen. 3) We shall determine the effects of Lyn and Fyn deficiencies on tolerance to double-stranded DNA using Ig transgenic mice developed by Martin Weigert and coworkers. 4) We shall determine the effects of Lyn and Fyn deficiencies on allosensitization by platelet transfusions to test the hypothesis that genetic affecting lymphocyte responsiveness may cause individuals to be more or less likely to make an alloantibody response following transfusions.

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

- **Project Title: VASCULAR COMPLICATIONS OF POLYCYSTIC KIDNEY DISEASE**

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

  Timing: Fiscal Year 2003; Project Start 01-JUN-2003; Project End 30-APR-2008

  Summary: (provided by applicant): Dr. Qian's long-term objective is to contribute to a better understanding of **kidney disease** pathophysiology, especially the vascular complications of autosomal dominant polycystic **kidney disease** (ADPKD). Her aim, over five-years, is to become a well-trained independent physician scientist with advance theoretical and technical knowledge in genetics and molecular and cellular biology through the implementation of this proposal. The candidate's mentor, Dr. Torres, is an expert in clinical and vascular aspects of ADPKD and her co-mentor, Dr. Harris, brings a detailed knowledge of ADPKD genetics. The third mentor, Dr. Farrugia, is an expert in Ca2+ homeostasis and will provide valuable guidance for that part of the

proposal. The particular focus of this proposal is to study the role of the ADPKD proteins, polycystin-1 and -2 in the vasculature and to determine if defects in these proteins are directly related to the vascular manifestations and hypertension associated with ADPKD. Preliminary studies have indicated that the polycystins are expressed in vascular smooth muscle cells (VSMC) and that they interact as a part of a polycystin complex that may play a role in maintaining intracellular Ca2+ The first two Specific Aims of the proposal are to examine the consequences of mutation to the murine Pkdl and Pkd2 genes, and over expression of the human protein in mouse, on the characteristics of VSMCs. These will be analyzed in vitro, as cultured VSMCs and in vivo, by study of the ultrastructure of the vasculature in the mouse mutants. Specific Aim 3 will identify components of a VSMC polycystin complex using imaging methods, co-immunoprecipitation and the yeast two- hybrid technique. The results of these studies will allow a VSMC polycystin complex to be defined and comparison made to corresponding complexes in epithelial cells. The final part of the proposal (Specific Aim 4) will examine the role of the polycystins in maintaining intracellular calcium homeostasis and analyze the consequences of Pkd1/2 mutation. Overall, the results from these studies should provide a clearer view of the function of the polycystins in VSMCs and the likely role that loss of these proteins may play in the vascular abnormalities and hypertension associated with ADPKD. This information will provide the basis for designing rational therapies for the treatment of these complications. This period of laboratory based study, plus the formalized career development program, is designed to train the candidate as a physician scientist with a unique expertise in vascular aspects of ADPKD.

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

- **Abnormal Sodium Pump Distribution During Renal Tubulogenesis in Congenital Murine Polycystic Kidney Disease.** by Avner ED, Sweeney WE Jr, Nelson WJ.; 1992 Aug 15;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=49727

[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.

- **Cellular Activation Triggered by the Autosomal Dominant Polycystic Kidney Disease Gene Product PKD2.** by Arnould T, Sellin L, Benzing T, Tsiokas L, Cohen HT, Kim E, Walz G.; 1999 May;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=84135
- **Cleavage of polycystin-1 requires the receptor for egg jelly domain and is disrupted by human autosomal-dominant polycystic kidney disease 1-associated mutations.** by Qian F, Boletta A, Bhunia AK, Xu H, Liu L, Ahrabi AK, Watnick TJ, Zhou F, Germino GG.; 2002 Dec 24;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=139255
- **CpG Island in the Region of an Autosomal Dominant Polycystic Kidney Disease Locus Defines the 5' End of a Gene Encoding a Putative Proton Channel.** by Gillespie GA, Somlo S, Germino GG, Weinstat-Saslow D, Reeders ST.; 1991 May 15;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=51644
- **Cystin, a novel cilia-associated protein, is disrupted in the cpk mouse model of polycystic kidney disease.** by Hou X, Mrug M, Yoder BK, Lefkowitz EJ, Kremmidiotis G, D'Eustachio P, Beier DR, Guay-Woodford LM.; 2002 Feb 15;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=150876
- **JunD protects against chronic kidney disease by regulating paracrine mitogens.** by Pillebout E, Weitzman JB, Burtin M, Martino C, Federici P, Yaniv M, Friedlander G, Terzi F.; 2003 Sep 15;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=193664
- **Kidney-specific inactivation of the KIF3A subunit of kinesin-II inhibits renal ciliogenesis and produces polycystic kidney disease.** by Lin F, Hiesberger T, Cordes K, Sinclair AM, Goldstein LS, Somlo S, Igarashi P.; 2003 Apr 29;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=154337
- **Mutations in a NIMA-related kinase gene, Nek1, cause pleiotropic effects including a progressive polycystic kidney disease in mice.** by Upadhya P, Birkenmeier EH, Birkenmeier CS, Barker JE.; 2000 Jan 4;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=26643
- **Nephrology: 4. Strategies for the care of adults with chronic kidney disease.** by Stigant C, Stevens L, Levin A.; 2003 Jun 10;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=156688
- **Polycystic kidney disease in patients on the renal transplant waiting list: trends in hematocrit and survival.** by Abbott KC, Agodoa LY.; 2002;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=122070
- **Polycystic kidney disease: In danger of being X-rated?** by Grantham JJ, Calvet JP.; 2001 Jan 30;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=33367
- **Polycystin, the Polycystic Kidney Disease 1 Protein, is Expressed by Epithelial Cells in Fetal, Adult, and Polycystic Kidney.** by Ward CJ, Turley H, Ong AC, Comley M, Biddolph S, Chetty R, Ratcliffe PJ, Gatter K, Harris PC.; 1996 Feb 20;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=39973
- **Polycystin-2, the protein mutated in autosomal dominant polycystic kidney disease (ADPKD), is a Ca2 +-permeable nonselective cation channel.** by Gonzalez-Perrett S,

Kim K, Ibarra C, Damiano AE, Zotta E, Batelli M, Harris PC, Reisin IL, Arnaout MA, Cantiello HF.; 2001 Jan 30;
http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=14729

- **Targeted Disruption of Bcl-2[alpha][beta] in Mice: Occurrence of Gray Hair, Polycystic Kidney Disease, and Lymphocytopenia.** by Nakayama K, Nakayama K, Negishi I, Kuida K, Sawa H, Loh DY.; 1994 Apr 26;
http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=43649
- **The polycystic kidney disease protein PKD2 interacts with Hax-1, a protein associated with the actin cytoskeleton.** by Gallagher AR, Cedzich A, Gretz N, Somlo S, Witzgall R.; 2000 Apr 11;
http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=18134
- **Trichosporon loubieri Infection in a Patient with Adult Polycystic Kidney Disease.** by Padhye AA, Verghese S, Ravichandran P, Balamurugan G, Hall L, Padmaja P, Fernandez MC.; 2003 Jan;
http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=149621

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

- **A controlled, prospective study of the effects of atorvastatin on proteinuria and progression of kidney disease.**
Author(s): Bianchi S, Bigazzi R, Caiazza A, Campese VM.
Source: American Journal of Kidney Diseases : the Official Journal of the National Kidney Foundation. 2003 March; 41(3): 565-70.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12612979&dopt=Abstract

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

- **A tuberous sclerosis patient with a large TSC2 and PKD1 gene deletion shows extrarenal signs of autosomal dominant polycystic kidney disease.**
  Author(s): Longa L, Brusco A, Carbonara C, Polidoro S, Scolari F, Valzorio B, Riegler P, Tardanico R, Migone N.
  Source: Contrib Nephrol. 1997; 122: 91-5. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9399046&dopt=Abstract

- **Acute visual loss in a child with autosomal recessive polycystic kidney disease: case report and review of the literature.**
  Author(s): Thomas WJ, Sahney S, Siegel LM.
  Source: J Aapos. 2003 June; 7(3): 217-20. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12825065&dopt=Abstract

- **Advancing chronic kidney disease care: new imperatives for recognition and intervention.**
  Author(s): Szromba C, Thies MA, Ossman SS.
  Source: Nephrology Nursing Journal : Journal of the American Nephrology Nurses' Association. 2002 December; 29(6): 547-59; Quiz 560-1. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12596604&dopt=Abstract

- **An efficient linkage analysis strategy for autosomal dominant polycystic kidney disease.**
  Author(s): Onoe T, Konoshita T, Miyagi K, Yamada K, Mutoh H, Koni I, Nomura H.
  Source: Clinical Nephrology. 2003 June; 59(6): 406-14.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12834171&dopt=Abstract

- **Analysis of long-term survival after revascularization in patients with chronic kidney disease presenting with acute coronary syndromes.**
  Author(s): Keeley EC, Kadakia R, Soman S, Borzak S, McCullough PA.
  Source: The American Journal of Cardiology. 2003 September 1; 92(5): 509-14.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12943868&dopt=Abstract

- **Anemia in chronic kidney disease and congestive heart failure.**
  Author(s): Silverberg DS, Wexler D, Blum B, Iaina A.
  Source: Blood Purification. 2003; 21(1): 124-30. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12596758&dopt=Abstract

- **Angiotensin II and the glomerulus: focus on diabetic kidney disease.**
  Author(s): Scholey JW.
  Source: Current Hypertension Reports. 2003 April; 5(2): 172-80. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12642018&dopt=Abstract

- **Angiotensinogen and angiotensin II type 1 receptor gene polymorphism in patients with autosomal dominant polycystic kidney disease: effect on hypertension and ESRD.**
  Author(s): Lee KB, Kim UK.
  Source: Yonsei Medical Journal. 2003 August 30; 44(4): 641-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12950120&dopt=Abstract

- **Anticoagulation in acute cardiac care in patients with chronic kidney disease.**
  Author(s): Reddan D, Szczech LA, O'Shea S, Califf RM.
  Source: American Heart Journal. 2003 April; 145(4): 586-94.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12679753&dopt=Abstract

- **Applying multiple interventions in chronic kidney disease.**
  Author(s): Barrett BJ.
  Source: Seminars in Dialysis. 2003 March-April; 16(2): 157-64. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12641881&dopt=Abstract

- **Association of mutation position in polycystic kidney disease 1 (PKD1) gene and development of a vascular phenotype.**
  Author(s): Rossetti S, Chauveau D, Kubly V, Slezak JM, Saggar-Malik AK, Pei Y, Ong AC, Stewart F, Watson ML, Bergstralh EJ, Winearls CG, Torres VE, Harris PC.
  Source: Lancet. 2003 June 28; 361(9376): 2196-201.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12842373&dopt=Abstract

- **Autosomal dominant polycystic kidney disease.**
  Author(s): Torres VE, Harris PC.
  Source: Nefrologia. 2003; 23 Suppl 1: 14-22. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12708359&dopt=Abstract

- **Autosomal dominant polycystic kidney disease: clinical and genetic aspects.**
  Author(s): Sessa A, Ghiggeri GM, Turco AE.
  Source: Journal of Nephrology. 1997 November-December; 10(6): 295-310. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9442442&dopt=Abstract

- **Autosomal dominant polycystic kidney disease: molecular genetics and pathophysiology.**
  Author(s): Sutters M, Germino GG.
  Source: The Journal of Laboratory and Clinical Medicine. 2003 February; 141(2): 91-101. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12577044&dopt=Abstract

- **Autosomal recessive polycystic kidney disease (ARPKD).**
  Author(s): Zerres K, Rudnik-Schoneborn S, Senderek J, Eggermann T, Bergmann C.
  Source: Journal of Nephrology. 2003 May-June; 16(3): 453-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12832752&dopt=Abstract

- **Autosomal recessive polycystic kidney disease. Clinical and genetic profile. (Review and a case report).**
  Author(s): Dimitrakov JD, Dimitrakov DI.
  Source: Folia Med (Plovdiv). 2003; 45(1): 5-7. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12943060&dopt=Abstract

- **Autosomal recessive polycystic kidney disease: improvement of renal function.**
  Author(s): Bosch BM, Plank C, Rascher W, Dotsch J.
  Source: European Journal of Pediatrics. 2003 June; 162(6): 438-9. Epub 2003 March 22.
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  Author(s): Provenzano R.
  Source: Manag Care. 2003 April; Spec No: 3-7; Discussion 17-20. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12751137&dopt=Abstract

- **Treatment of anemia in the diabetic patient with retinopathy and kidney disease.**
  Author(s): Sinclair SH, DelVecchio C, Levin A.
  Source: American Journal of Ophthalmology. 2003 May; 135(5): 740-3. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12719099&dopt=Abstract

- **Ultrasonographic study of pancreatic cysts in autosomal dominant polycystic kidney disease.**
  Author(s): Torra R, Nicolau C, Badenas C, Navarro S, Perez L, Estivill X, Darnell A.
  Source: Clinical Nephrology. 1997 January; 47(1): 19-22.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9021236&dopt=Abstract

- **Unilateral and segmental localised polycystic kidney disease.**
  Author(s): Gouldesbrough DR, Fleming S.
  Source: Journal of Clinical Pathology. 1998 September; 51(9): 703-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9930078&dopt=Abstract

- **Unilateral form of polycystic kidney disease.**
  Author(s): Branger B.
  Source: Nephrology, Dialysis, Transplantation : Official Publication of the European Dialysis and Transplant Association - European Renal Association. 1999 November; 14(11): 2775-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10534533&dopt=Abstract

- **Unilateral multicystic dysplastic kidney disease: defining the natural history. Anglia Paediatric Nephrourology Group.**
  Author(s): Sukthankar S, Watson AR.
  Source: Acta Paediatrica (Oslo, Norway : 1992). 2000 July; 89(7): 811-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10943963&dopt=Abstract

- **University of Miami Division of Clinical Pharmacology Therapeutic Rounds: managing hypertension in patients with kidney disease-implications for preservation of renal function.**
  Author(s): Preston RA, Fernandez L.
  Source: American Journal of Therapeutics. 1998 September; 5(5): 355-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10099077&dopt=Abstract

- **Unsuspected atherosclerotic renal artery stenosis causing renal failure in a patient with adult polycystic kidney disease.**
  Author(s): Makanjuola D, Reidy J, Scoble JE.
  Source: Nephrology, Dialysis, Transplantation : Official Publication of the European Dialysis and Transplant Association - European Renal Association. 1997 March; 12(3): 591-2.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9075150&dopt=Abstract

- **Urate homeostasis in polycystic kidney disease: comparison with chronic glomerulonephritic kidney.**
  Author(s): Mavromatidis K, Magoula I, Tsapas G.
  Source: Renal Failure. 2002 July; 24(4): 447-59.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12212824&dopt=Abstract

- **Uremia-related metabolic cardiac risk factors in chronic kidney disease.**
  Author(s): Madore F.
  Source: Seminars in Dialysis. 2003 March-April; 16(2): 148-56. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12641880&dopt=Abstract

- **Urinary tract infections per se do not cause end-stage kidney disease.**
  Author(s): Sreenarasimhaiah S, Hellerstein S.
  Source: Pediatric Nephrology (Berlin, Germany). 1998 April; 12(3): 210-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9630039&dopt=Abstract

- **Utility of ultrasonography in the diagnosis of autosomal dominant polycystic kidney disease in children.**
  Author(s): Gabow PA, Kimberling WJ, Strain JD, Manco-Johnson ML, Johnson AM.
  Source: Journal of the American Society of Nephrology : Jasn. 1997 January; 8(1): 105-10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9013454&dopt=Abstract

- **Value of magnetic resonance angiography for the detection of intracranial aneurysms in autosomal dominant polycystic kidney disease.**
  Author(s): Huston J 3rd, Torres VE, Sulivan PP, Offord KP, Wiebers DO.
  Source: Journal of the American Society of Nephrology : Jasn. 1993 June; 3(12): 1871-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8338918&dopt=Abstract

- **Variable renal disease progression in autosomal dominant polycystic kidney disease: a role for nitric oxide?**
  Author(s): Devuyst O.
  Source: Journal of Nephrology. 2003 May-June; 16(3): 449-52. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12832751&dopt=Abstract

- **Vocal cord paralysis and cystic kidney disease in Hajdu-Cheney syndrome.**
  Author(s): Fryns JP, Stinckens C, Feenstra L.
  Source: Clinical Genetics. 1997 April; 51(4): 271-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9184252&dopt=Abstract

- **Volumetric determination of progression in autosomal dominant polycystic kidney disease by computed tomography.**
  Author(s): Sise C, Kusaka M, Wetzel LH, Winklhofer F, Cowley BD, Cook LT, Gordon M, Grantham JJ.
  Source: Kidney International. 2000 December; 58(6): 2492-501.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11115083&dopt=Abstract

- **Volumetric measurement of renal cysts and parenchyma using MRI: phantoms and patients with polycystic kidney disease.**
  Author(s): Bae KT, Commean PK, Lee J.
  Source: Journal of Computer Assisted Tomography. 2000 July-August; 24(4): 614-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10966197&dopt=Abstract

- **Von Hippel-Lindau disease masquerading as autosomal dominant polycystic kidney disease.**
  Author(s): Chatha RK, Johnson AM, Rothberg PG, Townsend RR, Neumann HP, Gabow PA.
  Source: American Journal of Kidney Diseases : the Official Journal of the National Kidney Foundation. 2001 April; 37(4): 852-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11273887&dopt=Abstract

- **Von Hippel-Lindau disease: an important differential diagnosis of polycystic kidney disease.**
  Author(s): Browne G, Jefferson JA, Wright GD, Hughes AE, Doherty CC, Nevin NC, Keogh JA.
  Source: Nephrology, Dialysis, Transplantation : Official Publication of the European Dialysis and Transplant Association - European Renal Association. 1997 June; 12(6): 1132-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9198040&dopt=Abstract

- **Western New York Kidney Disease Project shows how disease management can work.**
  Author(s): Schorr W.
  Source: Nephrol News Issues. 2003 August; 17(9): 31-2. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12971223&dopt=Abstract

- **What is the role of decorin in diabetic kidney disease?**
  Author(s): Mogyorosi A, Ziyadeh FN.
  Source: Nephrology, Dialysis, Transplantation : Official Publication of the European Dialysis and Transplant Association - European Renal Association. 1999 May; 14(5): 1078-81. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10344340&dopt=Abstract

- **What, if any, is the appropriate neurological work-up for a child with autosomal dominant polycystic kidney disease and a family history of intra-cranial aneurysm?**
  Author(s): Robinson RO.
  Source: Pediatric Nephrology (Berlin, Germany). 1995 April; 9(2): 158.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7794708&dopt=Abstract

- **Whole blood-, plasma- and red blood cell glutathione and cysteine in patients with kidney disease and during hemodialysis.**
  Author(s): Jacobson SH, Moldeus P.
  Source: Clinical Nephrology. 1994 September; 42(3): 189-92.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7994938&dopt=Abstract

- **Why is chronic kidney disease the "spoiler" for cardiovascular outcomes?**
  Author(s): McCullough PA.
  Source: Journal of the American College of Cardiology. 2003 March 5; 41(5): 725-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12628713&dopt=Abstract

- **Wilms tumor and multicystic dysplastic kidney disease.**
  Author(s): Homsy YL, Anderson JH, Oudjhane K, Russo P.
  Source: The Journal of Urology. 1997 December; 158(6): 2256-9; Discussion 2259-60. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9366370&dopt=Abstract

CHAPTER 2. NUTRITION AND KIDNEY DISEASE

Overview

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

Finding Nutrition Studies on Kidney Disease

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

- **Antihypertensive efficacy of amlodipine in children with chronic kidney diseases.**
  Author(s): Division of Nephrology, University Children's Hospital, Inselspital, CH-3010 Bern, Switzerland.
  Source: von Vigier, R O Franscini, L M Bianda, N D Pfister, R Casaulta Aebischer, C Bianchetti, M G J-Hum-Hypertens. 2001 June; 15(6): 387-91 0950-9240
- **Clinical practice. Nondiabetic kidney disease.**
  Author(s): Division of Nephrology, Tufts-New England Medical Center, Boston, USA.
  Source: Levey, A S N-Engl-J-Med. 2002 November 7; 347(19): 1505-11 1533-4406
- **Evaluation and treatment of iron deficiency in patients with kidney disease.**
  Author(s): Fresnius Medical Care Central Dupage Dialysis Center, 25 N. Winfield Road, Winfield, IL 60190, USA. bickford119@juno.com
  Source: Bickford, A K Nutr-Clin-Care. 2002 Sep-October; 5(5): 225-30 1096-6781
- **Management of anemia in chronic kidney disease (predialysis) patients: nephrology nursing implications.**
  Author(s): Case Western Reserve University School of Medicine, USA.
  Source: Wish, J B Weigel, K A Nephrol-Nurs-J. 2001 June; 28(3): 341-5 1526-744X
- **Renal cyst ablation with n-butyl cyanoacrylate and iodized oil in symptomatic patients with autosomal dominant polycystic kidney disease: preliminary report.**
  Author(s): Department of Radiology, Seoul National University Hospital, 28 Yongon-Dong, Chongno-Gu, Seoul 110-744, Korea. kimsh@radcom.snu.ac.kr
  Source: Kim, S H Moon, M W Lee, H J Sim, J S Kim, S H Ahn, C Radiology. 2003 February; 226(2): 573-6 0033-8419
- **Salt intake and kidney disease.**
  Author(s): Nephrology and Dialysis Unit, San Giovanni Bosco Hospital, Turin, Italy. dialtoiv@tin.it
  Source: Boero, R Pignataro, A Quarello, F J-Nephrol. 2002 May-June; 15(3): 225-9 1120-3625
- **Systemic complications of chronic kidney disease. Pinpointing clinical manifestations and best management.**
  Author(s): Division of Nephrology, New England Medical Center, 750 Washington St, Box 5224, Boston, MA 02111, USA.
  Source: Obrador, Gregorio T Pereira, Brian J G Postgrad-Med. 2002 February; 111(2): 115-22; quiz 21 0032-5481
- **The African American Study of Kidney Disease and Hypertension (AASK): new findings.**
  Author(s): Division of Clinical Pharmacology and Hypertension, Medical College of Virginia of Virginia Commonwealth University, Richmond, VA 23298-0160, USA.
  Source: Sica, D A Douglas, J G J-Clin-Hypertens-(Greenwich). 2001 Jul-August; 3(4): 244-51 1524-6175

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 kidney disease; 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**

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

  Vitamin B6
  Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

- **Minerals**

  Angiotensin-Converting Enzyme (ACE) Inhibitors
  Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

- **Food and Diet**

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

  Carbo-Loading Diet
  Source: Healthnotes, Inc.; www.healthnotes.com

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

  Lamb and Mutton
  Source: Healthnotes, Inc.; www.healthnotes.com

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

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

CHAPTER 3. ALTERNATIVE MEDICINE AND KIDNEY DISEASE

Overview

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

The Combined Health Information Database

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

- **Soybeans: Good for Your Heart. Patient Education**

  Source: Advance for Nurse Practitioners. 10(5): 85. May 2002.

  Summary: This article provides information on the health benefits of soybeans and foods made from soybeans. The possible benefits that soy proteins may have on certain diseases, such as coronary heart disease, menopause, osteoporosis, cancer, allergies, diabetes, and **kidney disease,** are briefly noted. The article also describes the soy products currently available, including edamame, miso, tofu, soy nuts, tempeh, soy milk, soy sauce, and natto. It lists two Web sites for additional information on soybeans.

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 kidney disease 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 "kidney disease" (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 kidney disease:

- **"Giving back" on their own time for nearly four decades.**
  Author(s): Neumann ME.
  Source: Nephrol News Issues. 2003 January; 17(2): 26-7. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12629825&dopt=Abstract

- **Diet and kidney diseases in rats.**
  Author(s): Rao GN.
  Source: Toxicologic Pathology. 2002 November-December; 30(6): 651-6. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12512864&dopt=Abstract

- **Effects of antioxidants on kidney disease.**
  Author(s): Mune M, Otani H, Yukawa S.
  Source: Mechanisms of Ageing and Development. 2002 April 30; 123(8): 1041-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12044953&dopt=Abstract

- **Elevated bone turnover in rat polycystic kidney disease is not due to prostaglandin E2.**
  Author(s): Weiler H, Kovacs H, Nitschmann E, Fitzpatrick Wong S, Bankovic-Calic N, Ogborn M.
  Source: Pediatric Nephrology (Berlin, Germany). 2002 October; 17(10): 795-9. Epub 2002 August 10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12376805&dopt=Abstract

- **Evidence that soyasaponin Bb retards disease progression in a murine model of polycystic kidney disease.**
  Author(s): Philbrick DJ, Bureau DP, Collins FW, Holub BJ.
  Source: Kidney International. 2003 April; 63(4): 1230-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12631339&dopt=Abstract

- **Health care resource utilization and the impact of anemia management in patients with chronic kidney disease.**
  Author(s): London R, Solis A, Goldberg GA, Wade S, Ryu S.

Source: American Journal of Kidney Diseases : the Official Journal of the National Kidney Foundation. 2002 September; 40(3): 539-48.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12200806&dopt=Abstract

- **Palliative care in chronic kidney disease: peer mentoring program personalizes advance directives discussions.**
  Author(s): Perry E, Swartz J, Kelly G, Brown SL, Swartz RD.
  Source: Nephrol News Issues. 2003 July; 17(8): 28-31. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12882109&dopt=Abstract

- **Resveratrol, a component of wine and grapes, in the prevention of kidney disease.**
  Author(s): Bertelli AA, Migliori M, Panichi V, Origlia N, Filippi C, Das DK, Giovannini L.
  Source: Annals of the New York Academy of Sciences. 2002 May; 957: 230-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12074975&dopt=Abstract

Additional Web Resources

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

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

The following is a specific Web list relating to kidney disease; 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**

  Allergies
  Alternative names: Hay Fever
  Source: Prima Communications, Inc.www.personalhealthzone.com

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

  Anxiety and Panic Attacks
  Source: Prima Communications, Inc.www.personalhealthzone.com

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

  Benign Prostatic Hyperplasia
  Alternative names: Prostate Enlargement
  Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Herpes
Alternative names: Genital Herpes, Cold Sores
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

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

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

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

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

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

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

Menopausal Symptoms (Other Than Osteoporosis)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

Night Vision (Impaired)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

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

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

Reiter's Syndrome
Source: Integrative Medicine Communications; www.drkoop.com

Restless Legs Syndrome
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

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

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

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

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

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

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

Water Retention
Source: Integrative Medicine Communications; www.drkoop.com

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

- **Alternative Therapy**

Chelation Therapy
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,679,00.html

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

- **Chinese Medicine**

Shiwuwei Chenxiang Wan
Alternative names: Shiwuwei Chenxiang Pills; Shiwuwei Chenxiang Wan
(Shi Wu Wei Chen Xiang Wan)
Source: Pharmacopoeia Commission of the Ministry of Health, People's Republic of China

- **Herbs and Supplements**

5-htp (5-hydroxytryptophan)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

Ananas Comosus
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

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

Beta-carotene
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10103,00.html

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

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

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

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

Boldo
Alternative names: Peumus boldus
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

Butcher's Broom
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

Cat's Claw
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

Coenzyme Q10 (coQ10)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

Conjugated Linoleic Acid
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

Devil's Claw
Source: Prima Communications, Inc.www.personalhealthzone.com

DHEA (Dehydroepiandrosterone)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

Eicosapentaenoic Acid (EPA)
Source: Integrative Medicine Communications; www.drkoop.com

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

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

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

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

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

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

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

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

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

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

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

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

GLA (Gamma-Linolenic Acid)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

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

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

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

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

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

HMB (Hydroxymethyl Butyrate)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

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

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

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

Juniper
Alternative names: Juniperus communis
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Melatonin
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,804,00.html

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

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

Motherwort
Alternative names: Leonurus cardiaca
Source: Healthnotes, Inc.; www.healthnotes.com

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

N-Acetyl Cysteine (NAC)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

OPCS (Oligomeric Proanthocyanidins)
Source: Prima Communications, Inc.www.personalhealthzone.com

Ornithine Alpha-Ketoglutarate
Source: Prima Communications, Inc.www.personalhealthzone.com

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

PABA (Para-Aminobenzoic Acid)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

Pennyroyal
Alternative names: Hedeoma pulegoides, Mentha pulegium
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

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

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

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

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

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

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

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

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

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

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

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

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

SAMe (S-Adenosylmethionine)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

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

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

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

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

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

TMG (Trimethylglycine)
Source: Prima Communications, Inc.www.personalhealthzone.com

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

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

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

Uva Ursi
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10063,00.html

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

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

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

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

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

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

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

Yohimbe
Alternative names: Pausinystalia yohimbe
Source: Healthnotes, Inc.; www.healthnotes.com

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

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

General References

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

CHAPTER 4. DISSERTATIONS ON KIDNEY DISEASE

Overview

In this chapter, we will give you a bibliography on recent dissertations relating to kidney disease. We will also provide you with information on how to use the Internet to stay current on dissertations. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical dissertations that use the generic term "kidney disease" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on kidney disease, we have not necessarily excluded non-medical dissertations in this bibliography.

Dissertations on Kidney Disease

ProQuest Digital Dissertations, the largest archive of academic dissertations available, is located at the following Web address: **http://wwwlib.umi.com/dissertations**. From this archive, we have compiled the following list covering dissertations devoted to kidney disease. You will see that the information provided includes the dissertation's title, its author, and the institution with which the author is associated. The following covers recent dissertations found when using this search procedure:

- **A New Approach to Evaluate Risks to Life: a Case Study of End Stage Renal Disease (kidney Disease)** by Hondroyiannis, George B., PhD from Clark University, 1990, 116 pages
  http://wwwlib.umi.com/dissertations/fullcit/9026082
- **Bacterial Kidney Disease in Salmonid Fish: Development of Methods to Assess Immune Functions in Salmonid Fish during Infection by Renibacterium Salmoninarum** by Jansson, Eva; FilDr from Sveriges Lantbruksuniversitet (Sweden), 2002, 51 pages
  http://wwwlib.umi.com/dissertations/fullcit/f333457
- **Burden and Health in Caregivers of Persons with Kidney Disease** by Harris, Tammara Tonizcia; PhD from The University of Tennessee Center for the Health Sciences, 2003, 209 pages
  http://wwwlib.umi.com/dissertations/fullcit/3085398

- **Chronic Kidney Disease: Impact on the Child and Family and Strategies for Coping.** by Klein, Susan Jean Ditchett, PhD from University of Minnesota, 1975, 378 pages
  http://wwwlib.umi.com/dissertations/fullcit/7604055
- **Identity and Chronic Illness: Kidney Disease and Quality of Life** by Junco, Brenda; PhD from University of South Florida, 2003, 281 pages
  http://wwwlib.umi.com/dissertations/fullcit/3079990
- **The Treatment of Kidney Disease: an Analysis of Medical Care Process, Medical Care Structure and Patient Outcomes** by Evans, Roger Wayne, PhD from Duke University, 1979, 291 pages
  http://wwwlib.umi.com/dissertations/fullcit/8003620

Keeping Current

Ask the medical librarian at your library if it has full and unlimited access to the *ProQuest Digital Dissertations* database. From the library, you should be able to do more complete searches via **http://wwwlib.umi.com/dissertations**.

CHAPTER 5. CLINICAL TRIALS AND KIDNEY DISEASE

Overview

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

Recent Trials on Kidney Disease

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

- **Angiotensin-Converting Enzyme Gene Polymorphism and the Risk of Chronic Allograft Nephropathy**

  Condition(s): Kidney Disease

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Center for Research Resources (NCRR)

  Purpose - Excerpt: This study is intended to help doctors learn about the relationships between specific genetic makeup (gene markers) and the development of chronic rejection. This study is being done to see if there is a relationship between genetic patterns and the development of Chronic Allograft Nephropathy (CAN). Medical scientists also hope to learn more about how genetic differences between people determine their response to a drug or a disease by storing a small blood sample in a special "bank". This sample may be tested at some point in the future in an attempt to better understand the factors that may influence rejection, transplantation outcomes and transplant success rates.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00006328

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

- **Determination of Kidney Function**

  Condition(s): Kidney Disease

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

  Purpose - Excerpt: Much more about kidney disorders can be learned by determining kidney function. This research proposes to study the kidneys function by several parameters known as glomerular filtration rate (GFR), Renal Plasma Flow (RPF), and Glomerular Capillary Wall Permselectivity. The study will select patients suffering from different types of kidney diseases. These patients will be selected based on the presence of significant amounts of protein in their urine (proteinuria). Standard blood and urine tests are often unable to provide completely accurate information about the kidney. In order for researchers to have a more accurate idea of kidney function, they will use alternative tests. Test materials (para aminohippurate and inulin) will be injected into patients veins that provides information based on their filtration through the kidneys.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001978

- **Dynamic Aspects of Amino Acid Metabolism**

  Condition(s): Kidney Diseases

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Center for Research Resources (NCRR)

  Purpose - Excerpt: This protocol seeks to define aspects of intestinal and hepatic uptake and metabolism of several amino acids. The major hypothesis to be tested is that the splanchic bed (intestine and liver) conserves essential amino acids and metabolites while synthesizing and metabolizing nonessential amino acids. The aims of the study include defining the relative roles of enteral and hepatic extraction/metabolism in the disposition of glutamate, alanine, methionine and other amino acids. Emphasis will also be placed on studies of the transamination of alpha-ketoisocaproic acid (KIC) to leucine since this reaction is of potential importance in the design of nutritional regimens for patients with renal disease.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00005767

- **Evaluate the Survival Benefits of Zemplar versus Calcijex in Subjects w/ Stage V Chronic Kidney Disease on Hemodialysis**

  Condition(s): End-Stage Kidney Disease

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Abbott Laboratories

  Purpose - Excerpt: To evaluate the survival benefit associated with Zemplar therapy as compared to Calcijex for the treatment of secondary hyperparathyroidism in subjects with Stage V chronic kidney disease on hemodialysis as measured by time to death.

  Phase(s): Phase IV

Study Type: Observational

Contact(s): Julie Rock 847-937-3286 julie.rock@abbott.com

Web Site: http://clinicaltrials.gov/ct/show/NCT00062699

- **Evaluation of Autosomal Recessive Polycystic Kidney Disease and Congenital Hepatic Fibrosis**

  Condition(s): Polycystic Kidney, Autosomal Recessive

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Human Genome Research Institute (NHGRI)

  Purpose - Excerpt: This study will evaluate patients with autosomal recessive polycystic kidney disease (ARPKD) and congenital hepatic fibrosis (CHF). People with ARPKD develop kidney cysts and eventually kidney failure. Hypertension (high blood pressure), poor growth, and urinary infections are common symptoms. CHF is a specific type of liver disease associated with ARPKD. It involves fibrosis, or scarring, of the liver, which can lead to life-threatening complications, including internal bleeding of enlarged blood vessels called varices in the esophagus (food pipe). The goal of the study is to better understand the medical complications of ARPKD and CHF and identify characteristics that can help in the design of new treatments. Patients 6 months of age and older with ARPKD may be eligible for this 5- to 10-year study, excluding those who require frequent hospitalizations due to complications of end-stage renal disease or liver disease. Participants will undergo some or all of the following tests and procedures every 12 months during a 4- to 5-day hospital admission at the NIH Clinical Center: - Medical history and physical examination; 24-hour urine collection and blood tests to evaluate kidney and liver function; face and body photography to document growth and the effects of enlarged organs on posture; blood tests for basic research, including genetic studies related to ARPKD - Ultrasound of the abdomen to see changes in the kidneys, liver, spleen, and portal vein (vein leading to the liver); ultrasound of the heart in patients with hypertension. Ultrasound uses a probe held on the skin to send sound waves to organs. A computer converts the sound waves into images. - Magnetic resonance imaging (MRI) of the liver and kidneys. MRI uses a magnetic field and radio waves to scan organs while the patient lies still in a tunnel-like machine. - Electroencephalogram (EEG) in patients with portal hypertension to look for signs of hepatic encephalopathy. Electrodes are placed on the head to measure electrical activity of the brain (brain waves). - Cognitive function testing in patients with portal hypertension. Brain function is assessed through paper and pencil exercises that involve answering questions or drawing pictures. - X-rays and other tests, such as placement of intravenous lines, as needed for medical management - Endoscopy, if needed, to help prevent bleeding of esophageal varices. For this procedure, the patient is given medication for relaxation and sleep. Then, a tube with a light on the tip is advanced through the mouth down the food pipe and stomach to examine the organs and stop any bleeding. Results of tests performed, including information on the genetic cause of the ARPKD, will be provided the patient (or parent) if requested. In addition, medical data gathered on participants will be submitted to the ARPKD registry in Birmingham, Alabama. Identifying information will not be attached to the information.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00068224

- **Immune System Related Kidney Disease**

  Condition(s): Glomerulonephritis; Lupus Nephritis; Membranous Glomerulonephritis; Nephritis; Nephrotic Syndrome

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

  Purpose - Excerpt: Kidney diseases related to the immune system include, nephrotic syndrome, glomerulonephritis, membranous nephropathy, lupus nephritis, and nephritis associated with connective tissue disorders. This study will allow researchers to admit and follow patients suffering from autoimmune diseases of the kidney. It will attempt to provide information about the causes and specific abnormalities associated with autoimmune kidney disease. Patients with kidney disease as a result of their immune system, and patients with diseases of the immune system who may later develop kidney disease, will be potential subjects for this study. Patients will undergo a history and physical examination, and standard laboratory test to more closely understand the causes, signs, symptoms, and responses to medication of these diseases. Based on these evaluations the patients may qualify as candidates for other experimental studies. At any time these patients may be asked to submit blood or urine samples for further research.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001979

- **Monitoring for Tolerance to Kidney or Combined Kidney-Pancreas Transplants**

  Condition(s): Graft Rejection; Kidney Disease

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

  Purpose - Excerpt: This protocol facilitates the development of methods for determining whether transplant recipients have developed immune hyporesponsiveness or tolerance towards their allograft. These methods will involve the study of peripheral blood or biopsy tissue obtained at regular intervals from patients receiving kidney or combined kidney-pancreas allografts at the Warren G. Magnuson Clinical Center. In addition, patients that have previously received a kidney or combined kidney-pancreas allograft will be evaluated using assays requiring peripheral blood mononuclear cells and/or biopsies. Assays developed under this protocol will be used in subsequent protocols to assess the effects of immune modulating treatment regimens and may eventually be used to direct clinical care or guide the withdrawal of immunosuppressive agents. However, patients enrolled in this protocol will not have any change in treatment based solely on the assays developed without being enrolled in an additional study.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001858

- **Pirfenidone to Treat Kidney Disease (Focal Segmental Glomerulosclerosis)**

  Condition(s): Fibrosis; Focal Glomerulosclerosis; Kidney Failure; Nephrotic Syndrome; Proteinuria

Study Status: This study is currently recruiting patients.

Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Purpose - Excerpt: This study will examine the effectiveness of the drug pirfenidone in treating focal segmental glomerulosclerosis (FSGS). Patients with this disease have kidney fibrosis (scarring) and proteinuria (excessive excretion of protein in the urine). About half of patients with FSGS eventually require kidney dialysis or transplant. Steroids, which are currently used to treat the disease, are effective in only a minority of patients. Other drugs, such as cyclosporin and cyclophosphamide, improve proteinuria in a very small percentage of patients and have serious side effects. Patients with FSGS who wish to participate in this study will undergo pre-study evaluation with blood and urine tests. Patients must be on a stable dose of an ACE inhibitor (a drug that lowers blood pressure and reduces proteinuria) for at list 6 months before starting pirfenidone therapy. (Patients who are not already taking an ACE inhibitor will be started on the drug; those who cannot tolerate ACE inhibitors will be given a different drug.) Patients with elevated cholesterol will take a cholesterol-lowering drug. A diet containing approximately 1 gram of protein per kilogram of body weight per day will be recommended. Patients will take pirfenidone by mouth 3 times a day for 12 months. Blood and urine will be tested once a month, either at NIH or by the patient's local kidney specialist. They will collect two 24-hour urine samples at the beginning of the treatment period, at 2-month intervals throughout the study, and at a 6-month follow-up. Patients will also be asked to give three to five tubes of blood and urine samples for analysis during the study. In animal studies, pirfenidone improved kidney function and proteinuria and reduced kidney scarring in rats with a disease similar to FSGS. In human studies, pirfenidone improved breathing and survival in patients with lung fibrosis.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00001959

- **Pirfenidone: A New Drug to Treat Kidney Disease in Patients with Diabetes**

  Condition(s): Diabetes Mellitus; Diabetic Nephropathy

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Sharma, Kumar, M.D.; National Institutes of Health (NIH); National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); InterMune Pharmaceuticals

  Purpose - Excerpt: The purpose of this study is to determine whether a new investigational drug, pirfenidone, will be an effective therapy for diabetic patients with kidney dysfunction. Our hypothesis is that administration of pirfenidone to type 1 and type 2 diabetic patients with advanced kidney disease will lead to preservation of kidney function.

  Phase(s): Phase I; Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00063583

- **Safety and Efficacy of Zemplar Capsule in Reducing Serum iPTH Levels in Chronic Kidney Disease Subjects (daily dosing)**

  Condition(s): Renal Insufficiency, Chronic

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Abbott Laboratories

  Purpose - Excerpt: The objective of this study is to determine whether paricalcitol is safe and effective compared to placebo in reducing elevated serum PTH levels in patients with chronic kidney disease.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00048516

- **Steroid Treatment for Kidney Disease**

  Condition(s): Nephrosis; Focal Lipoid Glomerulosclerosis

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

  Purpose - Excerpt: Focal segmental glomerulosclerosis (FSGS) and minimal change disease are kidney diseases that are associated with increased excretion of protein in the urine. Approximately half of FSGS patients will lose kidney function within 8 years of diagnosis and will require dialysis. The purpose of this study is to determine whether intermittent oral steroid therapy can cause sustained remission of FSGS and MCD. Approximately 70 participants, including adults and children older than age 2, will be enrolled in this study. They will receive 48 doses of oral dexamethasone over a period of 48 weeks. One group will take two daily doses every 2 weeks; the other group will take four daily doses every 4 weeks. Doctors will monitor participants before, during, and after the steroid treatment with extensive exams and testing. At the completion of the study, researchers will evaluate the safety and efficacy of the drug treatment.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00065611

- **The Role of Connective Tissue Growth Factor in the Development of Kidney Disease After Organ Transplantation**

  Condition(s): Kidney Transplantation; MEDLINEplus consumer health information

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

  Purpose - Excerpt: This study will examine whether measurements of connective tissue growth factor (CTGF) and other cell proteins can identify which kidney transplant recipients are likely to develop chronic allograft nephropathy (CAN), a disease of the transplanted kidney. CAN may occur months to years after the transplant. The kidney becomes progressively scarred and eventually loses all function, so that dialysis or another transplant is needed. A better understanding of how CTGF and other proteins

are involved in the development of CAN may provide new targets for treating for the disease. Patients who are scheduled to receive a kidney or combined kidney-pancreas transplant or who have received a transplant recently (within 6 months) may be eligible for this study. Participants will be enrolled before the transplant, if possible, or after the transplant, and will undergo the following tests and procedures: - Physical examinations at the screening visit, at 1, 6, 12, and 24 months, and then once yearly. - Blood sample collections at the screening visit, at 1, 6, 12, 18, and 24 months and then once yearly. - Urine sample collections at the screening visit, at 1, 6, 12, 18, and 24 months and then once yearly. - Kidney biopsies at the beginning of the study, at 1, 6, 12, and 24 months, and then once a year for research purposes. Participants may refuse to have a research biopsy at any time during the study. Also, patients who are having a kidney biopsy for another reason at these time points will not have a second biopsy. The biopsy procedure takes about 15 minutes and is done in the hospital. The patient lies on his or her back and the skin over the transplanted kidney is cleaned with alcohol and iodine. The area is numbed with an injection of an anesthetic, and then a biopsy needle is placed through the kin. The biopsy may be repeated up to three times to get enough tissue to test for CAN. Patients lie flat for 4 hours after the procedure to reduce the risk of bleeding, and are observed for another 2 hours for possible complications.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00056784

- **Effectiveness of the Investigational Drug Campath-1H in Preventing Rejection of Transplanted Kidneys**

  Condition(s): Graft Rejection; Kidney Disease

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

  Purpose - Excerpt: This protocol will test a humanized monoclonal antibody known as Campath-1H for its ability to induce a state of permanent allograft acceptance, or tolerance, when administered in combination with a brief course of the immunosuppressive drug deoxyspergualin (DSG) at the time of human renal allotransplantation. Campath-1H is specific for the common lymphocyte and monocyte antigen CD52. Its administration temporarily depletes mature lymphocytes and some monocytes without altering neutrophils or hematopoietic stem cells. Deoxyspergualin inhibits the NFkB pathway thus preventing monocyte and macrophage activation. Recipients of living or cadaveric donor kidneys will be treated with one dose of Campath-1H prior to transplantation to insure that peripheral depletion is achieved at the time of graft reperfusion. Three subsequent doses of Campath-1H will be administered on the first, third and fifth days after the transplant to deplete passenger donor leukocytes and residual recipient cells that mobilize in response to the allograft. In addition, patients will be treated with DSG for 14 days beginning on the day prior to surgery. This trial expands on pilot studies at the NIH of 15 patients in which Campath was given alone at the time of transplantation. In those studies, excellent peripheral depletion occurred after just one dose of Campath though central depletion required additional dosing. This allowed for greatly reduced immunosuppression to be used to prevent rejection, but to date, all patients have required some immunosuppressive medication. It is hoped that the addition of DSG will eliminate the need for long-term immunosuppression. Patients will be followed closely in the post transplant period. If patients experience rejection, they will be treated with methylprednisolone and have

immunosuppression added using sirolimus as the predominant immunosuppressive agent. In the previous phase of this study without DSG, this maneuver has in all cases been successful in returning the allograft to normal function. In addition to evaluating graft function following transplantation, this protocol will also characterize and evaluate the function of the immune system and the composition of the T cell repertoire following the administration of Campath-1H and DSG, and during immune system recovery after transplantation.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00001984

- **Pegylated Interferon and Ribavarin to Treat Chronic Hepatitis C with and without Kidney Disease**

  Condition(s): Hepatitis C

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

  Purpose - Excerpt: This study will examine the effectiveness of pegylated interferon, or peginterferon (a long-acting form of alpha interferon) plus ribavirin in treating hepatitis C (genotype 1) infection with and without kidney disease. (Genotype 1 is a strain of hepatitis C virus that has a lower success rate of therapy.) Combination therapy with alpha interferon and ribavirin is the recommended treatment for hepatitis C infection in patients without kidney disease. However, it is not successful in all patients. An early predictor of who is or is not likely to respond to therapy would allow treatment to be stopped in non-responders within 2 to 4 weeks rather than 6 or 12 months. This study will determine whether early changes in viral levels with treatment predict the ultimate outcome. It will also compare responses in patients without and with kidney disease to better evaluate problems of therapy in the latter group. Ribavirin is not given to people with kidney disease because of possible severe drug side effects. However, because patients with kidney disease are poor treatment responders and because ribavirin increases the success of therapy in patients without kidney disease 2- to 3-fold, however, this study will look for a dose of the drug that can safely be given to patients with kidney disease. Patients 18 years of age and older with hepatitis C, genotype 1, with or without kidney disease may be eligible for this study. Candidates will be screened with a medical history and physical evaluation, blood tests, symptom questionnaires, 24-hour urine collection, chest X-ray, electrocardiogram, and liver ultrasound. A liver biopsy (removal of a small piece of liver tissue) will be done in patients who have not had one within the last year. Additional procedures, such as eye examination, treadmill stress test, hearing test, or others may be required depending on the individual's medical condition. Patients without kidney disease will be randomly assigned to one of two treatment groups: Group A will take both peginterferon (by injection under the skin once a week) and ribavirin (capsules by mouth) from the start of therapy; Group B will start treatment with peginterferon alone and add ribavirin after 4 weeks. Patients with kidney disease (Group C) will start with peginterferon alone and add ribavirin 4 weeks later. All patients will be admitted to the NIH Clinical Center for a few days when treatment starts in order to draw blood at precise intervals (6, 12, 24, 48, and 72 hours after the first peginterferon injection) for measurements of viral levels. Blood will then be drawn once a week for 4 weeks (just before each injection) to determine how rapidly viral levels decrease with treatment and to measure blood levels of interferon and

ribavirin. After 4 weeks of therapy, patients will have a blood test and check of symptoms and side effects every 4 weeks for 24 weeks (every 2 weeks for Group C patients until the optimum ribavirin dose is found) and then every 8 weeks for the remainder of the study. They will have a physical examination and urine test every 12 weeks. Patients will be tested for hepatitis virus RNA after 24 weeks of therapy to determine if they are a responder or non-responder. Responders will be advised to continue therapy for a full 48 weeks to ensure a continued response when treatment stops. Non-responders-whose chances for a lasting response are estimated at only 2%-will be offered the option to continue treatment, to stop treatment and continue being followed without treatment, or to enroll in other studies of non-responders. At the end of the 72-week treatment and follow-up, patients will have the same blood and urine tests as were done at the beginning of the study and a repeat liver ultrasound.

Phase(s): Phase IV

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00028093

- **Safety and Efficacy of Zemplar Capsule in Reducing Serum IPTH Levels in Chronic Kidney Disease Subjects (Three times weekly)**

  Condition(s): Renal Insufficiency, Chronic

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): Abbott Laboratories

  Purpose - Excerpt: The objective of this study is to determine whether paricalcitol is safe and effective compared to placebo in reducing elevated serum PTH levels in patients with chronic kidney disease.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00048438

- **A Study of Saquinavir Soft Gel Capsules (SGC) Used in Combination With Two Other Anti-HIV Drugs in Patients with HIV-Associated Kidney Disease**

  Condition(s): HIV Infections; AIDS-Associated Nephropathy

  Study Status: This study is completed.

  Sponsor(s): Hoffmann-La Roche

  Purpose - Excerpt: The purpose of this study is to compare the safety and effectiveness of saquinavir SGC plus stavudine (d4T) plus lamivudine (3TC) with that of saquinavir SGC plus nelfinavir plus d4T in patients with HIV-associated kidney disease. This study examines whether these drug combinations are effective in preventing kidney disease from progressing to a stage where it is immediately life threatening. This study also examines the effect these drug combinations have on the level of HIV detected in these patients. Finally, this study evaluates the drug level (the amount of drug found in the body) of these two combinations in patients with kidney disease.

  Phase(s): Phase III

  Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00002397

- **A Study of Zidovudine in HIV-Infected Patients with Kidney Problems**

  Condition(s): HIV Infections; Kidney Disease

  Study Status: This study is terminated.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: To determine how zidovudine (AZT) for the treatment of HIV infection is metabolized and excreted or eliminated in patients with infected or diseased kidneys. To determine the influence of hemodialysis and establish dose guidelines. AZT is the only antiviral agent with demonstrated effectiveness in patients with severe HIV infection. Persons with HIV infection may have additional health problems, one of which is a diseased kidney due to infection of the kidney, or side effects of therapy. The benefits and risks of AZT in patients with diseased kidneys are unknown. It is hoped that this study will allow further understanding of the metabolism and excretion of AZT in patients with **kidney disease.** AZT pharmacokinetics will be studied in patients with mild, moderate, and severe renal disorders

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000685

- **Evaluation of New Test Method to Measure Kidney Function**

  Condition(s): Kidney Disease

  Study Status: This study is completed.

  Sponsor(s): National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

  Purpose - Excerpt: This study will test the accuracy of a new "Fast GFR" (glomerular filtration rate) test to evaluate kidney function. Accurate assessment of kidney function is important in many clinical situations, including detecting **kidney disease** early, determining appropriate drug dosages, deciding when to begin dialysis, and evaluating heart and kidney organ donors and recipients. The current GFR test is used mostly for research purposes, as it is too costly and complicated for general medical use. Another significant drawback to its use in diagnosing acute kidney failure is the time it takes (3 to 24 hours) to complete, since effective therapy for this condition requires its detection as soon as possible. The Fast GFR, by comparison, takes only 45 minutes. Patients 6 years old and older with **kidney disease** or with impaired kidney function caused by abnormal heart function or swelling-from congestive heart failure, severe infections, swelling from fluid accumulation, fluid in the abdomen, or burns-may be eligible for this study. Patients will undergo both the standard and the Fast GFR tests, described below, to evaluate the accuracy of the new test. Fast GFR: Two catheters (thin flexible tubes) are placed into two arm veins, one for injecting iothalamate-an agent commonly used in CT scanning and blood vessel imaging-and the other for collecting blood samples. Baseline blood and urine samples are collected and then 0.5 milliliter (ml) iothalamate is injected into a vein. Blood samples are collected at 5, 10, 15, 20, 30, and 45 minutes in adults and at 5, 15, and 45 minutes in children. Urine is collected at 45 minutes. The size of the bladder is measured using ultrasound to determine if the

bladder has completely emptied. Standard GFR: Iothalamate (1 ml) is injected under the skin. Blood samples are collected at 60, 90, 120, 180 and 240 minutes. (A heparin lock is used to avoid multiple needle sticks.) Urine is collected at 60, 90, 120, 180 and 240 minutes. The size of the bladder is measured using ultrasound to determine if the bladder has completely emptied.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00026715

- **Safety and Efficacy Study of LJP 394 (abetimus sodium) to treat lupus kidney disease**

  Condition(s): Immunologic Diseases; Autoimmune Diseases; Systemic Lupus Erythematosus; Lupus Nephritis; Lupus Glomerulonephritis

  Study Status: This study is completed.

  Sponsor(s): La Jolla Pharmaceutical Company

  Purpose - Excerpt: The purpose of this study is to determine whether LJP 394 (abetimus sodium) is safe and effective in delaying and reducing renal flares in patients with lupus nephritis.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00035308

Keeping Current on Clinical Trials

The U.S. National Institutes of Health, through the National Library of Medicine, has developed ClinicalTrials.gov to provide current information about clinical research across the broadest number of diseases and conditions.

The site was launched in February 2000 and currently contains approximately 5,700 clinical studies in over 59,000 locations worldwide, with most studies being conducted in the United States. ClinicalTrials.gov receives about 2 million hits per month and hosts approximately 5,400 visitors daily. To access this database, simply go to the Web site at **http://www.clinicaltrials.gov/** and search by "kidney disease" (or synonyms).

While ClinicalTrials.gov is the most comprehensive listing of NIH-supported clinical trials available, not all trials are in the database. The database is updated regularly, so clinical trials are continually being added. The following is a list of specialty databases affiliated with the National Institutes of Health that offer additional information on trials:

- For clinical studies at the Warren Grant Magnuson Clinical Center located in Bethesda, Maryland, visit their Web site: **http://clinicalstudies.info.nih.gov/**
- For clinical studies conducted at the Bayview Campus in Baltimore, Maryland, visit their Web site: **http://www.jhbmc.jhu.edu/studies/index.html**
- For cancer trials, visit the National Cancer Institute: **http://cancertrials.nci.nih.gov/**

- For eye-related trials, visit and search the Web page of the National Eye Institute: **http://www.nei.nih.gov/neitrials/index.htm**
- For heart, lung and blood trials, visit the Web page of the National Heart, Lung and Blood Institute: **http://www.nhlbi.nih.gov/studies/index.htm**
- For trials on aging, visit and search the Web site of the National Institute on Aging: **http://www.grc.nia.nih.gov/studies/index.htm**
- For rare diseases, visit and search the Web site sponsored by the Office of Rare Diseases: **http://ord.aspensys.com/asp/resources/rsch_trials.asp**
- For alcoholism, visit the National Institute on Alcohol Abuse and Alcoholism: **http://www.niaaa.nih.gov/intramural/Web_dicbr_hp/particip.htm**
- For trials on infectious, immune, and allergic diseases, visit the site of the National Institute of Allergy and Infectious Diseases: **http://www.niaid.nih.gov/clintrials/**
- For trials on arthritis, musculoskeletal and skin diseases, visit newly revised site of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health: **http://www.niams.nih.gov/hi/studies/index.htm**
- For hearing-related trials, visit the National Institute on Deafness and Other Communication Disorders: **http://www.nidcd.nih.gov/health/clinical/index.htm**
- For trials on diseases of the digestive system and kidneys, and diabetes, visit the National Institute of Diabetes and Digestive and Kidney Diseases: **http://www.niddk.nih.gov/patient/patient.htm**
- For drug abuse trials, visit and search the Web site sponsored by the National Institute on Drug Abuse: **http://www.nida.nih.gov/CTN/Index.htm**
- For trials on mental disorders, visit and search the Web site of the National Institute of Mental Health: **http://www.nimh.nih.gov/studies/index.cfm**
- For trials on neurological disorders and stroke, visit and search the Web site sponsored by the National Institute of Neurological Disorders and Stroke of the NIH: **http://www.ninds.nih.gov/funding/funding_opportunities.htm#Clinical_Trials**

CHAPTER 6. PATENTS ON KIDNEY DISEASE

Overview

Patents can be physical innovations (e.g. chemicals, pharmaceuticals, medical equipment) or processes (e.g. treatments or diagnostic procedures). The United States Patent and Trademark Office defines a patent as a grant of a property right to the inventor, issued by the Patent and Trademark Office.[9] Patents, therefore, are intellectual property. For the United States, the term of a new patent is 20 years from the date when the patent application was filed. If the inventor wishes to receive economic benefits, it is likely that the invention will become commercially available within 20 years of the initial filing. It is important to understand, therefore, that an inventor's patent does not indicate that a product or service is or will be commercially available. The patent implies only that the inventor has "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States. While this relates to U.S. patents, similar rules govern foreign patents.

In this chapter, we show you how to locate information on patents and their inventors. If you find a patent that is particularly interesting to you, contact the inventor or the assignee for further information. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical patents that use the generic term "kidney disease" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on kidney disease, we have not necessarily excluded non-medical patents in this bibliography.

Patents on Kidney Disease

By performing a patent search focusing on kidney disease, you can obtain information such as the title of the invention, the names of the inventor(s), the assignee(s) or the company that owns or controls the patent, a short abstract that summarizes the patent, and a few excerpts from the description of the patent. The abstract of a patent tends to be more technical in nature, while the description is often written for the public. Full patent descriptions contain much more information than is presented here (e.g. claims, references, figures, diagrams, etc.). We will tell you how to obtain this information later in the chapter. The following is an

[9]Adapted from the United States Patent and Trademark Office:
http://www.uspto.gov/web/offices/pac/doc/general/whatis.htm.

example of the type of information that you can expect to obtain from a patent search on kidney disease:

- **Bis (benzimidazole) derivatives serving as potassium blocking agents**

  Inventor(s): Jensen; Bo Skaaning (Copenhagen S, DK), Olesen; S.o slashed.ren Peter (Klampenborg, DK), Peters; Dan (Arlov, DK), Str.o slashed.b.ae butted.k; Dorte (Farum, DK), Teuber; Lene (V.ae butted.rl.o slashed.se, DK)

  Assignee(s): Neurosearch A/S (Ballerup, DK)

  Patent Number: 6,194,447

  Date filed: July 2, 1999

  Abstract: This invention relates to novel potassium channel blocking agents, and their use in the preparation of pharmaceutical compositions.Moreover the invention is directed to pharmaceutical compositions useful for the treatment or alleviation of diseases or disorders associated with the activity of potassium channels, in particular asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic **kidney disease,** bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory diarrhoea, ischaemia, cerebral ischaemia, ischaemic hearth disease, angina pectoris, coronary hearth disease, traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression.

  Excerpt(s): This invention relates to novel potassium channel blocking agents, and their use in the preparation of pharmaceutical compositions. Moreover the invention is directed to pharmaceutical compositions useful for the treatment or alleviation of diseases or disorders associated with the activity of potassium channels, in particular asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic **kidney disease,** bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory diarrhoea, ischaemia, cerebral ischaemia, ischaemic hearth disease, angina pectoris, coronary hearth disease, traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression. Ion channels are transmembrane proteins, which catalyze the transport of inorganic ions across cell membranes. The ion channels participate in processes as diverse as the generation and timing of action potentials, synaptic transmissions, secretion of hormones, contraction of muscles, etc.

  Web site: http://www.delphion.com/details?pn=US06194447__

- **Genes associated with diseases of the kidney**

  Inventor(s): Azimzai; Yalda (Hayward, CA), Klingler; Tod M. (San Carlos, CA), Volkmuth; Wayne (Menlo Park, CA), Walker; Michael G. (Sunnyvale, CA), Yue; Henry (Sunnyvale, CA)

  Assignee(s): Incyte Genomics, Inc. (Palo Alto, CA)

  Patent Number: 6,277,574

  Date filed: April 9, 1999

  Abstract: The invention provides novel kidney disease-associated genes and polypeptides encoded by those genes. The invention also provides expression vectors, host cells, and antibodies. The invention also provides methods for diagnosing, treating or preventing diseases of the kidney.

  Excerpt(s): The invention relates to nine genes associated with diseases of the kidney as identified by their coexpression with genes known to be associated with renal disorders. The invention also relates to polypeptides encoded by these genes and to the use of these amino acid and nucleic acid sequences in the diagnosis, prognosis, prevention, treatment, and evaluation of therapies for diseases of the kidney. The kidneys excrete waste and contribute to maintenance of homeostasis by regulating blood pH, electrolyte levels and blood pressure. Renal failure or dysfunction is the cause of several diseases whose clinical manifestations are typically hyper- or hypo-tension. These diseases include Bartter's syndrome, Gitelman syndrome, autosomal dominant polycystic **kidney disease,** and nephrolithiasis. Treatment with antibiotics such as gentamicin, tobramycin, or amikacin can lead to tubular necrosis with consequent risk of acute renal failure in as much as 25% of patients. A cumulative dose of 2 to 3 grams amphotericin B is likewise nephrotoxic. Cyclosporine, an immunosuppressant given to organ transplant patients, is also nephrotoxic. The molecular basis for the nephrotoxicity of these and other compounds is not understood, although calbindin D levels appear to be a useful diagnostic marker signaling cyclosporine-induced nephrotoxicity (Aicher et al. (1998) Electrophoresis 19:1998-2003). Similarly, reductions in urinary excretion of proteins such as Tamm-Horsfall protein, beta 2 microglobin, and urinary retinol binding protein, appear to be diagnostic for nephrctoxicity when induced by certain chemotherapeutic agents including ifosfamide and cisplatinum (MacLean et al. (1998) Cancer Chemother. Pharmacol. 41:413-6; Tokuc et al. (1997) J. Exp. Clin. Cancer Res. 16:227-30).

  Web site: http://www.delphion.com/details?pn=US06277574__

- **Growth-promoting proteins and peptides for kidney epithelial cells**

  Inventor(s): Toback; F. Gary (Chicago, IL), Walsh-Reitz; Margaret M. (River Forest, IL)

  Assignee(s): Arch Development Corporation (Chicago, IL)

  Patent Number: 6,096,706

  Date filed: November 20, 1997

  Abstract: Novel growth peptides derived from protein factors having molecular weights of about 22 and 45 kDa stimulate mitogenic activity of epithelial, but not fibroblastic cells, in particular, kidney epithelial cells. A source of the factors is scrape-wounded kidney epithelial cells in culture. Synthetic peptides having sixteen amino acids or less, in particular a hexapeptide, YPQGNH (SEQ ID NO: 2) maintain the mitogenic activity. The peptide AQPYPQGNHEASYG (14-Ser) (SEQ ID NO: 15) is effective in reversing

acute renal failure in animals. The growth-promoting characteristics of the 22 and 45 kDa proteins and the peptides are useful in treating and diagnosing patients with **kidney disease.** Nucleotide sequences that encode the factor are useful to develop probes to locate similar factors, to identify genetic disorders involving the factor, and to produce the factor by genetic recombinant methods. The nucleotide sequences and fragments thereof, are also useful for diagnosis and treatment of kidney disorders.

Excerpt(s): Novel growth peptides derived from protein factors having molecular weights of about 22 and 45 kDa stimulate mitogenic activity of epithelial, but not fibroblastic cells, in particular, kidney epithelial cells. Acute renal failure is a serious disease associated with high mortality for which no "real" treatment currently exists. Acute renal failure is defined as the abrupt disruption of previously normal kidney function. It is caused by a wide variety of mechanisms including circulatory failure (shock), vascular blockade, glomerulonephritis, and obstruction to urine flow. In addition it can occur following surgery, trauma, sepsis, or with certain medications, particularly antibiotics and anticancer agents. In 1985 some 140,000 Americans were hospitalized with acute renal failure (see 1990 Long Range Plan). The average cost of treatment associated with these cases was over $9000. Based on the growth in the disease over the past several years and normal inflation, it was estimated that currently some 240,000 patients develop acute renal failure annually at a cost of over $10,000 per patient. That translated to a staggering total cost to the U.S. healthcare system of almost $2.5 billion per year.

Web site: http://www.delphion.com/details?pn=US06096706__

- **HMVAB41**

  Inventor(s): Gallagher; Kathleen Theresa (Willow Grove, PA), Hurle; Mark R (Norristown, PA), Kikly; Kristine Kay (Linfield, PA)

  Assignee(s): SmithKline Beecham Corporation (Philadelphia, PA)

  Patent Number: 5,932,446

  Date filed: November 26, 1997

  Abstract: HMVAB41 polypeptides and polynucleotides and methods for producing such polypeptides by recombinant techniques are disclosed. Also disclosed are methods for utilizing HMVAB41 polypeptides and polynucleotides in the design of protocols for the treatment of cancer, inflammation, autoimmunity, allergy, asthma, rheumatoid arthritis, CNS inflammation, cerebellar degeneration, Alzheimer's disease, Parkison's disease, multiple sclerosis, amylotrophic lateral sclerosis, head injury damage, and other neurological abnormalities, septic shock, sepsis, stroke, osteoporosis, osteoarthritis, ischemia reperfusion injury, cardiovascular disease, **kidney disease,** liver disease, ischemic injury, myocardial infarction, hypotension, hypertension, AIDS, myelodysplastic syndromes and other hematologic abnormalities, aplastic anemia, male pattern bladness, and bacterial, fungal, protozoan and viral infections, among others, and diagnostic assays for such conditions.

  Excerpt(s): This invention relates to newly identified polynucleotides, polypeptides encoded by them and to the use of such polynucleotides and polypeptides, and to their production, hereinafter referred to as HMVAB41. The invention also relates to inhibiting or activating the action of such polynucleotides and polypeptides. The drug discovery process is currently undergoing a fundamental revolution as it embraces `functional genomics`, that is, high throughput genome- or gene-based biology. This approach is

rapidly superceding earlier approaches based on `positional cloning`. A phenotype, that is a biological function or genetic disease, would be identified and this would then be tracked back to the responsible gene, based on its genetic map position. Functional genomics relies heavily on the various tools of bioinformatics to identify gene sequences of potential interest from the many molecular biology databases now available. There is a continuing need to identify and characterise further genes and their related polypeptides/proteins, as targets for drug discovery. This indicates that HMVAB41 related genes have an established, proven history as therapeutic targets. Clearly there is a need for identification and characterization of further members of this family which can play a role in preventing, ameliorating or correcting dysfunctions or diseases, including, but not limited to, cancer, inflammation, autoimmunity, allergy, asthma, rheumatoid arthritis, CNS inflammation, cerebellar degeneration, Alzheimer's disease, Parkinson's disease, multiple sclerosis, amylotrophic lateral sclerosis, head injury damage, and other neurological abnormalities, septic shock, sepsis, stroke, osteoporosis, osteoarthritis, ischemia reperfusion injury, cardiovascular disease, **kidney disease,** liver disease, ischemic injury, myocardial infarction, hypotension, hypertension, AIDS, myelodysplastic syndromes and other hematologic abnormalities, aplastic anemia, male pattern baldness, and bacterial, fungal, protozoan and viral infections.

Web site: http://www.delphion.com/details?pn=US05932446__

- **Human requiem**

  Inventor(s): Gross; Mitchell S (Wayne, PA), Hurle; Mark Robert (Norristown, PA), Kikly; Kristine Kay (Linfield, PA)

  Assignee(s): SmithKline Beecham Corporation (Philadelphia, PA)

  Patent Number: 5,919,660

  Date filed: June 24, 1997

  Abstract: Human REQUIEM polypeptides and DNA (RNA) encoding such REQUIEM and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such REQUIEM for the treatment of a susceptibility to viral infection, tumorogenesis and to diseases and defects in the control embryogenesis and tissue homeostasis, and the nucleic acid sequences described above may be employed in an assay for ascertaining such susceptibility. Antagonists against such REQUIEM and their use as a therapeutic to treat Alzheimer's disease, Parkinson's disease, rheumatoid arthritis, septic shock, sepsis, stroke, CNS inflammation, osteoporosis, ischemia reperfusion injury, cell death associated with cardiovascular disease, polycystic **kidney disease,** apoptosis of endothelial cells in cardiovascular disease, degenerative liver disease, MS, ALS, cererbellar degeneration, ischemic injury, myocardial infarction, AIDS, myelodysplastic syndromes, aplastic anemia, male pattern baldness, and head injury damage are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to mutations in the nucleic acid sequences and altered concentrations of the polypeptides. Also disclosed are diagnostic assays for detecting mutations in the polynucleotides encoding REQUIEM polypeptide and for detecting altered levels of the polypeptide in a host.

  Excerpt(s): This invention relates, in part, to newly identified polynucleotides and polypeptides; variants and derivatives of the polynucleotides and polypeptides; processes for making the polynucleotides and the polypeptides, and their variants and derivatives; agonists and antagonists of the polypeptides; and uses of the polynucleotides, polypeptides, variants, derivatives, agonists and antagonists. In

particular, in these and in other regards, the invention relates to polynucleotides and polypeptides of a human homologue of murine requiem gene, hereinafter referred to as "REQUIEM". Hematopoietic stem cell proliferation, differentiation and apoptosis, are regulated by various growth factors and cytokines (Metcalf, D., Science 254, 529-531 (1992) and Vaux et al., Nature 335, 440-442 (1988)). Such cells committed to the myeloid lineage express high affinity receptors for GM-CSF1 and IL-3 (Miyajima et al., Blood 82,1960-1973 (1993)). Moreover, such cells develop a requirement for GM-CSF or IL-3 to survive and undergo apoptosis in response to GM-CSF or IL-3 deprivation (Williams et al., Nature 343, 76-79 (1990)). Hematopoietic cells are not unique in their requirement for growth factors for survival. Throughout development, cells of all lineages require proper signals to grow and differentiate. Failure to receive these signals often results in death of the cells by apoptosis. Even in the adult organism there is constant renewal and/or maintence of cells that requires growth factors and cytokines. Inappropriate cessation of signals from these growth factors may result in apoptosis thereby causing disfunction or disease.

Web site: http://www.delphion.com/details?pn=US05919660__

- **Human SDR2 cDNA clone**

  Inventor(s): Albone; Earl Francis (Conshohocken, PA), Kikly; Kristine Kay (Linfield, PA)

  Assignee(s): SmithKline Beecham Corporation (Philadelphia, PA)

  Patent Number: 6,090,579

  Date filed: December 16, 1997

  Abstract: SDR2 polypeptides and polynucleotides and methods for producing such polypeptides by recombinant techniques are disclosed. Also disclosed are methods for utilizing SDR2 polypeptides and polynucleotides in the design of protocols for the treatment of cancer, inflammation, autoimmunity, allergy, asthma, rheumatoid arthritis, CNS inflamation, cerebellar degeneration, Alzheimer's disease, Parkinsons disease, multiple sclerosis, amylotrophic lateral sclerosis, head injury damage, and other neurological abnormalities, septic shock, sepsis, stroke, osteoporosis, osteoarthritis, ischemia reperfusion injury, cardiovascular disease, **kidney disease,** liver disease, ischemic injury, myocardial infarction, hypotension, hypertension, AIDS, myelodysplastic syndromes and other hematologic abnormalities, aplastic anemia, male pattern baldness, and bacterial, fungal, protozoan and viral infections, among others, and diagnostic assays for such conditions.

  Excerpt(s): This invention relates to newly identified polynucleotides, polypeptides encoded by them and to the use of such polynucleotides and polypeptides, and to their production. More particularly, the polynucleotides and polypeptides of the present invention relate to 6-TM family, hereinafter referred to as SDR2 (stromal-cell derived receptor). The invention also relates to inhibiting or activating the action of such polynucleotides and polypeptides. Murine SDR2 was cloned from a bone marrow stromal cell line using a signal sequence trap method (Shirozu, M., et al., Genomics 37:273-280, 1996). Murine SDR2 contains a signal sequence and has six putative transmembrane spanning domains. Other six transmembrane spanning proteins function as ion transporters (Becker, D., et al., PNAS 93:8123-8128, 1996), water channel proteins (Misaka, T., et al., FEBS Lett. 381:208-212, 199; Jung, J. S., et al., PNAS 91:13052-13056, 1994), iron transporters (Dix, D. R., et al., JBC 269:26092-26099, 1994) or have been linked to cellular activation and division (Gaugitsch, H. W., et al., JBC 267:11267-11273, 1992). This indicates that the 6-TM family has an established, proven history as

therapeutic targets. Clearly there is a need for identification and characterization of further members of 6-TM family which can play a role in preventing, ameliorating or correcting dysfunctions or diseases, including, but not limited to, cancer, inflammation, autoimmunity, allergy, asthma, rheumatoid arthritis, CNS inflammation, cerebellar degeneration, Alzheimer's disease, Parkinson's disease, multiple sclerosis, amylotrophic lateral sclerosis, head injury damage, and other neurological abnormalities, septic shock, sepsis, stroke, osteoporosis, osteoarthritis, ischemia reperfusion injury, cardiovascular disease, **kidney disease,** liver disease, ischemic injury, myocardial infarction, hypotension, hypertension, AIDS, myelodysplastic syndromes and other hematologic abnormalities, aplastic anemia, male pattern baldness, and bacterial, fungal, protozoan and viral infections. In one aspect, the invention relates to SDR2 polypeptides and recombinant materials and methods for their production. Another aspect of the invention relates to methods for using such SDR2 polypeptides and polynucleotides. Such uses include the treatment of cancer, inflammation, autoimmunity, allergy, asthma, rheumatoid arthritis, CNS inflammation, cerebellar degeneration, Alzheimer's disease, Parkinson's disease, multiple sclerosis, amylotrophic lateral sclerosis, head injury damage, and other neurological abnormalities, septic shock, sepsis, stroke, osteoporosis, osteoarthritis, ischemia reperfusion injury, cardiovascular disease, **kidney disease,** liver disease, ischemic injury, myocardial infarction, hypotension, hypertension, AIDS, myelodysplastic syndromes and other hematologic abnormalities, aplastic anemia, male pattern baldness, and bacterial, fungal, protozoan and viral infections, among others. In still another aspect, the invention relates to methods to identify agonists and antagonists using the materials provided by the invention, and treating conditions associated with SDR2 imbalance with the identified compounds. Yet another aspect of the invention relates to diagnostic assays for detecting diseases associated with inappropriate SDR2 activity or levels.

Web site: http://www.delphion.com/details?pn=US06090579__

- **Identification of polycystic kidney disease gene, diagnostics and treatment**

  Inventor(s): Glucksmann; Maria Alexandra (Somerville, MA), Reeders; Stephen (Newtonville, MA), Schneider; Michael (Boston, MA)

  Assignee(s): Brigham and Women's Hospital (Boston, MA), Millenium Pharmaceuticals (Cambridge, MA)

  Patent Number: 5,891,628

  Date filed: June 2, 1995

  Abstract: The present invention relates to the identification of the autosomal dominant polycystic **kidney disease** (PKD) gene and high throughput assays to identify compounds that interfere with PKD activity. Interfering compounds that inhibit the expression, synthesis and/or bioactivity of the PKD gene product can be used therapeutically to treat polycystic **kidney disease.**

  Excerpt(s): The present invention relates to the identification of the gene, referred to as the PKD1 gene, mutations in which are responsible for the vast majority of cases involving autosomal dominant polycystic **kidney disease** (ADPKD). The PKD1 gene, including the complete nucleotide sequence of the gene's coding region are presented. Further, the complete PKD1 gene product amino acid sequence and protein structure and antibodies directed against the PKD1 gene product are also presented. Additionally, the present invention relates to therapeutic methods and compositions for the treatment of ADPKD symptoms. Methods are also presented for the identification of compounds

that modulate the level of expression of the PKD1 gene or the activity of mutant PKD1 gene product, and the evaluation and use of such compounds in the treatment of ADPKD symptoms. Still further, the present invention relates to prognostic and diagnostic, including prenatal, methods and compositions for the detection of mutant PKD1 alleles and/or abnormal levels of PKD1 gene product or gene product activity. Autosomal dominant polycystic **kidney disease** (ADPKD) is among the most prevalent dominant human disorders, affecting between 1 in 1,000 and 1 in 3,000 individuals worldwide (Dalgaard, O. Z., 1957, Acta. Med. Scand. 158:1-251). The major manifestation of the disorder is the progressive cystic dilation of renal tubules (Gabow, P. A., 1990, Am. J. Kidney Dis. 16:403-413), leading to renal failure in half of affected individuals by age 50. Although studies of kidneys from ADPKD patients have demonstrated a number of different biochemical, structural and physiological abnormalities, the disorder's underlying causative biochemical defect remains unknown. Biochemical abnormalities which have been observed have involved proteinsorting, the distribution of cell membrane markers within renal epithelial cells, extracellular matrix, ion transport, epithelial cell turnover, and epithelial cell proliferation. The most carefully documented of these findings are abnormalities in the composition of tubular epithelial cells, and a reversal of the normal polarized distribution of cell membrane proteins, such as the Na.sup.+ /K.sup.+ ATPase (Carone, F. A. et al., 1994, Lab. Inv. 70:437-448.).

Web site: http://www.delphion.com/details?pn=US05891628__

- **Inhibition of cyst formation by cytoskeletal specific drugs**

  Inventor(s): Woo; David D. L. (Los Angeles, CA)

  Assignee(s): The Regents of the University of California (Oakland, CA)

  Patent Number: 5,789,189

  Date filed: May 22, 1995

  Abstract: The invention provides a method of producing a culture of polycystic kidney cells which form cysts in vitro. A cell culture of polycystic kidney cells is also provided. A method for screening an agent in vitro to determine the effectiveness of the agent in treating polycystic **kidney disease** is disclosed. Further, a method of treating a mammal having polycystic **kidney disease** by administering a pharmaceutical composition is provided.

  Excerpt(s): The present invention relates to cystic diseases. More specifically, the invention relates to the use of a culture of cells that form cysts in vitro, to a method of screening for agents which can treat such diseases, and to pharmacological treatments of the diseases. The cytoskeleton plays an important role in the growth, division, and migration of eukaryotic cells. Changes in cellular morphology, the repositioning of internal organelles, and cellular migration all depend on complex networks of protein filaments that traverse the cytoplasm. These protein filaments fall into three main categories according to their size: microtubules, intermediate filaments, and microfilaments. Both microtubules and microfilaments are made of globular subunits which can quickly polymerize and depolymerize in the cell resulting in movement and morphological changes. Intermediate filaments are made of fibrous protein subunits and tend to be more stable with longer half-lives than most microtubules and microfilaments.

  Web site: http://www.delphion.com/details?pn=US05789189__

- **Interleukin-1.beta. converting enzyme like apoptotic protease-6**

  Inventor(s): Dixit; Vishva M. (AnnArbor, MI), He; Wei-Wu (Columbia, MD), Kikly; Kristine K. (Linfield, PA), Ruben; Steven M. (Olney, MD)

  Assignee(s): Smithkline Beecham Corporation (Philadelphia, PA)

  Patent Number: 6,010,878

  Date filed: May 8, 1997

  Abstract: Human ICE LAP-6 polypeptides and DNA (RNA) encoding such ICE LAP-6 and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such ICE LAP-6 for the treatment of a susceptibility to viral infection, tumorogenesis and to diseases and defects in the control embryogenesis and tissue homeostasis, and the nucleic acid sequences described above may be employed in an assay for ascertaining such susceptibility. Antagonists against such ICE LAP-6 and their use as a therapeutic to treat Alzheimer's disease, Parkinson's disease, rheumatoid arthritis, septic shock, sepsis, stroke, chronic inflammation, acute inflammation, CNS inflammation, osteoporosis, ischemia reperfusion injury, cell death associated with cardiovascular disease, polycystic **kidney disease,** apoptosis of endothelial cells in cardiovascular disease, degenerative liver disease, MS, ALS, cererbellar degeneration, ischemic injury, myocardial infarction, AIDS, myelodysplastic syndromes, aplastic anemia, male pattern baldness, and head injury damage are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to mutations in the nucleic acid sequences and altered concentrations of the polypeptides. Also disclosed are diagnostic assays for detecting mutations in the polynucleotides encoding the interleukin-1 beta converting enzyme apoptosis proteases and for detecting altered levels of the polypeptide in a host.

  Excerpt(s): This invention relates, in part, to newly identified polynucleotides and polypeptides; variants and derivatives of the polynucleotides and polypeptides; processes for making the polynucleotides and the polypeptides, and their variants and derivatives; agonists and antagonists of the polypeptides; and uses of the polynucleotides, polypeptides, variants, derivatives, agonists and antagonists. In particular, in these and in other regards, the invention relates to polynucleotides and polypeptides of human interleukin-1 beta converting enzyme apoptosis protease-6, hereinafter referred to as "ICE LAP-6". It has recently been discovered that an interleukin-1.beta. converting enzyme (ICE) is responsible for cleaving pro-IL-1.beta. into mature and active IL-1.beta. and is also responsible for programmed cell death (or apoptosis), which is a process through which organisms get rid of unwanted cells. In the nematode Caenorhabditis elegans, a genetic pathway of programmed cell death has been identified (Ellis, R. E., et al. Annu. Rev. Cell Biol., 7:663-698 (1991)). Two genes, ced-3 and ced-4, are essential for cells to undergo programmed cell death in C. elegans (Ellis, H. M., and Horvitz, H. R., Cell, 44:817-829 (1986)). It is becoming apparent that a class of cysteine proteases homologous to Caenorhabditis elegans Ced-3 play the role of "executioner" in the apoptotic mechanism (Martin, S. J., and Green, D. R. (1995) Cell 82, 349-352; Chinnaiyan, A. a. D., VM. (1996) Current Biology 6; Henkart, P. (1996) Immunity 4, 195-201). Recessive mutations that eliminate the function of these two genes prevent normal programmed cell death during the development of C. elegans. The known vertebrate counterpart to ced-3 protein is ICE. The overall amino acid identity between ced-3 and ICE is 28%, with a region of 115 amino acids (residues 246-360 of ced-3 and 164-278 of ICE) that shows the highest identity (43%). This region contains a conserved pentapeptide, QACRG (SEQ ID NO:10) (residues 356-360 of ced-3), which contains a cysteine known to be essential for ICE function.

Web site: http://www.delphion.com/details?pn=US06010878__

- **Interleukin-1 beta converting enzyme like apoptotic protease-7**

  Inventor(s): Dixit; Vishva M. (Ann Arbor, MI), Kikly; Kristine K. (Linfield, PA), Ni; Jian (Rockville, MD), Rosen; Craig A. (Laytonsville, MD), Ruben; Steven M. (Olney, MD)

  Assignee(s): Human Genome Sciences, Inc. (Rockville, MD), Smithkline Beecham Corporation (Philadelphia, PA), The Regents of the University of Michigan (Ann Arbor, MI)

  Patent Number: 6,008,042

  Date filed: May 7, 1997

  Abstract: Human ICE LAP-7 polypeptides and DNA (RNA) encoding such ICE LAP-7 and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such ICE LAP-7 for the treatment of a susceptibility to viral infection, tumorogenesis and to diseases and defects in the control embryogenesis and tissue homeostasis, and the nucleic acid sequences described above may be employed in an assay for ascertaining such susceptibility. Antagonists against such ICE LAP-7 and their use as a therapeutic to treat Alzheimer's disease, Parkinson's disease, rheumatoid arthritis, septic shock, sepsis, stroke, chronic inflammation, acute inflammation, CNS inflammation, osteoporosis, ischemia reperfusion injury, cell death associated with cardiovascular disease, polycystic **kidney disease,** apoptosis of endothelial cells in cardiovascular disease, degenerative liver disease, MS, ALS, cererbellar degeneration, ischemic injury, myocardial infarction, AIDS, myelodysplastic syndromes, aplastic anemia, male pattern baldness, and head injury damage are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to mutations in the nucleic acid sequences and altered concentrations of the polypeptides. Also disclosed are diagnostic assays for detecting mutations in the polynucleotides encoding the interleukin-1 beta converting enzyme apoptosis proteases and for detecting altered levels of the polypeptide in a host.

  Excerpt(s): Apoptosis, or programmed cell death (PCD), is a genetically regulated mechanism with a central role in both metazoan development and homeostasis. (Raff, 1992; Steller, 1995). The cell death machinery is conserved throughout evolution (Vaux et al., 1994) and is composed of several distinct parts including effectors, inhibitors and activators (Chinnaiyan and Dixit, 1996; Steller, 1995). Invertebrate model systems have been invaluable in identifying and characterizing the genes that control apoptosis. (Hengartner, 1996). While numerous candidate genes have been identified, how they interact to execute the apoptotic program is poorly understood. It is becoming apparent that cysteine proteases related to the Caenorhabditis elegans cell death gene ced-3 represent the effector components of the apoptotic machinery. The first mammalian homolog of CED-3 identified was interleukin-1.beta. converting enzyme (ICE). (Yuan et al., 1993). Overexpression of ICE or CED-3 in Rat-1 fibroblasts induced apoptosis, suggesting that ICE was functionally, as well as structurally, related to CED-3. (Miura et al., 1993). However, such evidence is only a correlation, as ectopic expression of a number of proteases, including chymotrypsin, proteinase K and trypsin, cause significant apoptosis. (Williams and Henkart, 1994). Further studies suggested that proteases related to ICE, rather than ICE itself, may play a more important role in the apoptotic mechanism. First, a number of cell types stably secrete mature IL-1.beta. without undergoing apoptosis. Second, ICE-deficient mice, although unable to generate active IL-1.beta., fail to exhibit a prominent cell death defective phenotype,(Kuida et al.,

1995; Li et al., 1995). Third, in an in vitro model of apoptosis, condemned phase extracts prepared from chicken DU249 cells failed to cleave the primary substrate of ICE, pro-IL-1b. (Lazebnik et al., 1994). Instead, a proteolytic activity in these extracts, termed prICE, cleaved the DNA repair enzyme poly (ADP-ribose) polymerase (PARP) into signature apoptotic fragments. (Lazebnik et al., 1994). Purified ICE failed to cleave PARP (Lazebnik et al., 1994; Tewari et al., 1995), suggesting that prICE was distinct from ICE.

Web site: http://www.delphion.com/details?pn=US06008042__

- **Kidney disease detection and treatment**

  Inventor(s): Comper; Wayne D. (Victoria, AU)

  Assignee(s): Monash University (Victoria, AU)

  Patent Number: 6,447,989

  Date filed: October 12, 1999

  Abstract: A method is disclosed for diagnosing early stage of a disease in which an intact protein found in urine is an indicator of the disease. The method includes assaying urine sample to detect the presence of modified protein using either immunological or non-immunological technique. Methods for preventing and treating the disease are also disclosed.

  Excerpt(s): The present invention relates to methods of detecting an early stage of renal disease and/or renal complications of a disease. The invention also relates to preventing and treating the disease. The appearance of excess protein such as albumin in the urine is indicative of **kidney disease.** Diabetic nephropathy is such a disease. By the time the excess albumin is detected, **kidney disease** has progressed, possibly to a stage where it is irreversible and treatment has little effect. Therefore it is an object of the invention to provide a test that is more sensitive than the currently known radioimmunoassay to detect such a disease as early as possible so that the disease can be either prevented or a treatment protocol commenced early on in the disease. Specific proteinuria, and in particular, albuminuria (micro- and macro-), is a marker of disease including renal disease (glomerulonephritis, bacterial and viral glomerulonephritides, IgA nephropathy and Henoch-Schonlein Purpura, membranoproliferative glomerulonephritis, membranous nephropathy, Sjogren's syndrome, diabetic nephropathy, nephrotic syndrome (minimal change disease, focal glomerulosclerosis and related disorders), acute renal failure, acute tubulointerstitial nephritis, pyelonephritis, GU tract inflammatory disease, Pre-clampsia, renal graft rejection, leprosy, reflux nephropathy, nephrolithiasis), genetic renal disease (medullary cystic, medullar sponge, polycystic **kidney disease** (autosomal dominant polycystic **kidney disease,** autosomal recessive polycystic **kidney disease,** tuborous sclerosis), von Hippel-Lindau disease, familial thin-glomerular basement membrane disease, collagen III glomerulopathy, fibronectin glomerulopathy, Alport's syndrome, Fabry's disease, Nail-Patella Syndrome, congenital urologic anomalies), monoclonal gammopathies (multiple myeloma, amyloidosis and related disrders), febrile illness (familial Mediterannean fever, HIV infection--AIDS), inflammatory disease (systemic vasculitides (polyarteritis nodosa, Wegener's granulomatosis, polyarteritis, necrotizing and crescentic glomerulonephritis), polymyositis-dermatomyositis, pancreatitis, rheumatoid arthritis, systemic lupus erythematosus, gout), blood disorders (sickle cell disease, thrombotic thrombocytopenia purpura, hemolytic-uremic syndrome, acute corticol necrosis, renal thromboembolism), trauma and surgery (extensive injury, burns, abdominal and vascular surgery, induction of anaesthesia), drugs (penicillamine, steroids) and drug abuse, malignant disease

(epithelial (lung, breast), adenocarcinoma (renal), melanoma, lymphoreticular, multiple myeloma), circulatory disease (myocardial infarction, cardiac failure, peripheral vascular disease, hypertension, coronary heart disease, non-atherosclerotic cardiovascular disease, atherosclerotic cardiovascular disease), skin disease (psoriasis, systemic sclerosis), respiratory disease (COPD, obstructive sleep apnoea, hypoia at high altitude) and endocrine disease (acromegaly, diabetes mellitus, and diabetes insipidus).

Web site: http://www.delphion.com/details?pn=US06447989__

- **Phosphocholinate cardenolides**

  Inventor(s): Chasalow; Fred I. (San Carlos, CA)

  Assignee(s): Kerix, L.L.C. (San Carlos, CA)

  Patent Number: 6,130,211

  Date filed: January 21, 1999

  Abstract: Disclosed herein are cardenolides and related compounds covalently linked to phosphocholine moieties and pharmaceutical formulations comprising such compounds. Also disclosed herein are methods for treating hypertension, premenstrual syndrome (PMS), preeclampsia and polycystic **kidney disease** using the compounds.

  Excerpt(s): This invention is related to cardenolides and related compounds covalently linked to phosphocholine moieties, pharmaceutical formulations comprising such compounds and their therapeutic and diagnostic use. Digoxin, digitalis and related cardiotonic agents act on the heart in a variety of ways resulting in an increase in the force of contraction (a positive inotropic effect), a slowing in the rate of atrioventricular conduction thereby leading to improved hemodynamics and renal function. Such agents are useful in treating congestive heart disease and atrial fibrillation. Congestive heart disease is characterized by an incomplete emptying of blood from the heart during ventricular contraction, which leads to an enlargement of the heart. When congestive heart disease is treated with cardiac glycosides there is a reduction of heart rate, a more complete filling of the ventricules, and the size of the heart decreases and begins to return to normal. Atrial fibrillation is a condition in which the atria contract much more often then the ventricules, causing the lower heart chambers to be bombarded by impulses. The ventricules respond by weakly and inefficiently contracting. When used to treat atrial fibrillation, cardiac glycosides depress the conduction rate, slowing the rate of ventricular contraction and reestablishing a synchronous and effective heart beat.

  Web site: http://www.delphion.com/details?pn=US06130211__

- **Polycystic kidney disease gene and protein**

  Inventor(s): Burn; Timothy (Northborough, MA), Connors; Timothy (Hopkinton, MA), Dackowski; William (Hopkinton, MA), Germino; Gregory (Baltimore, MD), Klinger; Katherine (Sudbury, MA), Landes; Gregory (Northborough, MA), Qian; Feng (Baltimore, MD)

  Assignee(s): Genzyme Corporation (Framingham, MA), Johns Hopkins University (Baltimore, MD)

  Patent Number: 6,071,717

  Date filed: June 4, 1996

Abstract: The present invention involves isolated nucleic acid encoding human PKD1, and sequences derived therefrom. The invention also encompasses vectors comprising these nucleic acids, host cells transformed with the vectors, and methods for producing PKD1 protein or fragments thereof. In another aspect, the invention involves isolated oligonucleotides that hybridize only to the authentic expressed PKD1 gene, and not to PKD1 homologues. In yet another aspect, the invention involves isolated mutant PKD1 genes, and their cDNA cognates. Further provided are isolated oligonucleotides that discriminate between normal and mutant versions of the PKD1 gene. Methods and compositions for treating APKD or disease conditions having the characteristics of APKD are also provided.

Excerpt(s): The present invention pertains to the diagnosis and treatment of polycystic **kidney disease** in humans, using DNA sequences derived from the human PKD1 gene and the protein or proteins encoded by that gene. Autosomal dominant polycystic **kidney disease** (APKD), also called adult-onset polycystic **kidney disease,** is one of the most common hereditary disorders in humans, affecting approximately one individual in a thousand. The prevalence in the United States is greater than 500,000, with 6,000 to 7,000 new cases detected yearly (Striker et al., Am. J. Nephrol., 6:161-164, 1986; Iglesias et al., Am. J. Kid. Dis., 2:630-639, 1983). The disease is considered to be a systemic disorder, characterized by cyst formation in the ductal organs such as kidney, liver, and pancreas, as well as by gastrointestinal, cardiovascular, and musculoskeletal abnormalities, including colonic diverticulitis, berry aneurysms, hernias, and mitral valve prolapse (Gabow et al., Adv. Nephrol., 18:19-32, 1989; Gabow, New Eng. J. Med., 329:332-342, 1993). The most prevalent and obvious symptom of APKD, however, is the formation of kidney cysts, which result in grossly enlarged kidneys and a decrease in renal-concentrating ability. Hypertension and endocrine abnormalities are also common in APKD patients, appearing even before symptoms of renal insufficiency. In approximately half of APKD patients, the disease progresses to end-stage renal disease; accordingly, APKD is responsible for 4-8% of the renal dialysis and transplantation cases in the United States and Europe (Proc. European Dialysis and Transplant Assn., Robinson and Hawkins, eds., 17:20, 1981). Thus, there is a need in the art for diagnostic and therapeutic tools to reduce the incidence and severity of this disease.

Web site: http://www.delphion.com/details?pn=US06071717__

- **Regeneration of kidney tissue and use of autocrine growth factors**

  Inventor(s): Gluck; Stephen L. (St. Louis, MO), Toback; F. Gary (Chicago, IL), Walsh-Reitz; Margaret M. (River Forest, IL)

  Assignee(s): ARCH Development Corporation (Chicago, IL)

  Patent Number: 5,821,218

  Date filed: December 15, 1995

  Abstract: Autocrine growth factors and isoforms of those factors have been identified, isolated, purified and manipulated. Nucleic acid segments coding for the factors, and antibodies directed to the factors are also aspects of the present invention. The effect of these growth factors on cells is to enhance their growth by increasing mitogenesis. In particular, the growth factors stimulate kidney epithelial cell growth. The growth factors differ from others previously reported in their molecular weights and other properties, for example, resistance to denaturation by dithiothreitol. Methods of preparation and use of the factors are also described. The growth factors are released from kidney

epithelial cells by short exposures to a low-sodium environment. The factors have potential for treatment of **kidney disease.**

Excerpt(s): The present invention relates to the identification, isolation and purification of autocrine growth factors, and to nucleic acid segments coding for the growth factors. The present invention also relates to methods of preparing the factors, including recombinant genetic technology, and to use of the growth factors to enhance cell growth, in particular, renal epithelial cell growth. Cellular growth enhancement is useful in treating **kidney disease.** Acute renal failure refers to the abrupt disruption of previously normal kidney function. This serious clinical condition is due to a wide variety of mechanisms including circulatory failure (shock), vascular blockage, glomerulonephritis, and obstruction to urine flow. Acute renal failure frequently arises as a complication of abdominal or vascular surgery. Also, due to continued improvements in prenatal care, low birth weight, high-risk neonates may now survive lung and heart problems, only to die from complications of acute renal failure caused by infection or drug toxicity. Of particular clinical importance are cases of acute renal failure associated with trauma, sepsis, postoperative complications, or medication, particularly antibiotics. (National Center for Health Statistics, 1985, Table 1, National Institute of Health, 1990). Population data from the United States in 1985 further illustrate the nature of the problem. Acute renal failure was cited as a contributing cause in 26,922 deaths. The condition affects people of all ages, but those 65 years and older are almost five times more likely to be hospitalized for acute renal failure than those ages 45 to 64. Nearly two-thirds of all hospitalizations for acute renal failure occur in persons 65 years and older. Of those in that age group, black Americans were nearly twice as likely as white Americans to be hospitalized for acute renal failure. Acute renal failure is the most costly kidney or urologic condition requiring hospitalization. In 1985 there were 139,134 hospitalizations to for the disease at a cost of $1.3 billion, or $9,329 per hospital discharge.

Web site: http://www.delphion.com/details?pn=US05821218__

- **Screening methods for compounds useful in the treatment of polycystic kidney disease**

  Inventor(s): Burrow; Christopher R. (New York, NY), Wilson; Patricia D. (New York, NY)

  Assignee(s): Mount Sinai School of Medicine of New York University (New York, NY)

  Patent Number: 6,638,726

  Date filed: October 12, 2000

  Excerpt(s): The present invention provides cell-based screening assays designed to identify agents that regulate the activity of the polycystic **kidney disease** proteins encoded by the PKD-1 and PKD-2 genes and that may be useful in the treatment of polycystic **kidney disease.** The assays of the invention comprise the contacting of genetically engineered cells expressing a mutant or truncated PKD gene product with a test agent and assaying for a decrease in the PKD-mediated mutant phenotype. Characteristics associated with such a mutant phenotype include increased adherence to type I collagen coated surfaces; apical expression of NaK-ATPase on the cell membrane; increased expression of.beta.-2-NaK-ATPase; and decreased focal adhesion kinase (FAK) incorporation into focal adhesion complexes, inability to form tubular structures in a gel matrix and decreased cell motility. To facilitate the screening methods of the invention, cells may be genetically engineered to express epitope tagged PKD gene products

and/or epitope tagged PKD interacting proteins (PKD-IP). Such interacting proteins include, for example, focal adhesion complex proteins such as FAK, paxillin, vinculin, talin and the like. Autosomal dominant polycystic **kidney disease** (ADPKD) is the most common lethal genetic disease inherited as a dominant trait in humans, with a prevalence of 1:1,000 live births. The disease afflicts approximately 6 million people world-wide, and accounts for 5-7% of all patients on dialysis in the United States (Gabow, 1984, Ann. Intern. Med. 101:238-247). Mutations in the PKD-1 gene account for 85% of ADPKD, while mutations in the PKD-2 gene account for 10% of the disease. In both cases, ADPKD is characterized by progressive, massive cystic enlargement of renal tubules resulting from increased proliferation, aberrant secretion, altered membrane protein polarity, and extracellular matrix abnormalities correlated with a failure to down-regulate certain fetal genes after birth (Wilson, 1996, In Polycystic **Kidney Disease,** Oxford Clinical Nephrology Series, Watson M. L. and Torres V.E. eds. p. 124-163). Approximately 50% of patients who inherit a mutant PKD-1 gene will develop end stage renal failure, typically in the 5 th decade of life, necessitating renal replacement therapy by dialysis or transplantation. Since progression is usually slow and is a consequence of gradual loss of renal function as cysts continue to enlarge and destroy intervening normal renal tubules, this presents a window of opportunity for potential drug therapies that would inhibit cyst expansion.

Web site: http://www.delphion.com/details?pn=US06638726__

- **Substituted pyrido[3,2-d]pyrimidines capable of inhibiting tyrosine kinases of the epidermal growth factor receptor family**

  Inventor(s): Bridges; Alexander James (Saline, MI), Denny; William Alexander (Auckland, NZ), Fry; David (Ypsilanti, MI), Kraker; Alan (Ann Arbor, MI), Meyer; Robert Frederick (Ann Arbor, MI), Rewcastle; Gordon William (Auckland, NZ), Thompson; Andrew Mark (Auckland, NZ)

  Assignee(s): Warner-Lambert Company (Morris Plains, NJ)

  Patent Number: 6,084,095

  Date filed: March 6, 1997

  Abstract: Novel 4-substituted amino pyrido [3,2-d]pyrimidine inhibitors of epidermal growth factor receptor family of tyrosine kinases are described, as well as pharmaceutical compositions of the same, which are useful in treating proliferative diseases such as cancer, synovial pannus invasion in arthritis, psoriasis, vascular restenosis and angiogenesis and additionally useful in the treatment of pancreatitis and **kidney disease** as well as a contraceptive agent.

  Excerpt(s): The present invention relates to bicyclic heteroaromatic compounds which inhibit the epidermal growth factor receptor and related receptors and, in particular, their tyrosine kinase enzymic activity. Cancer is generally a disease of the intracellular signalling system, or signal transduction mechanism. Cells receive instructions from many extracellular sources, instructing them to either proliferate or not to proliferate. The purpose of the signal transduction system is to receive these and other signals at the cell surface, get them into the cell, and then pass the signals on to the nucleus, the cytoskeleton, and transport and protein syntheses machinery. The most common cause of cancer is a series of defects, either in these proteins, when they are mutated, or in the regulation of the quantity of the protein in the cell such that it is over or under produced. Most often, there are key lesions in the cell which lead to a constitutive state whereby the cell nucleus receives a signal to proliferate, when this signal is not actually

present. This can occur through a variety of mechanisms. Sometimes the cell may start to produce an authentic growth factor for its own receptors when it should not, the so-called autocrine loop mechanism. Mutations to the cell surface receptors, which usually signal into the cell by means of tyrosine kinases, can lead to activation of the kinase in the absence of ligand, and passing of a signal which is not really there. Alternatively, many surface kinases can be overexpressed on the cell surface leading to an inappropriately strong response to a weak signal. There are many levels inside the cell at which mutation or overexpression can lead to the same spurious signal arising in the cell, and there are many other kinds of signalling defect involved in cancer. This invention touches upon cancers which are driven by the three mechanisms just described, and which involve cell surface receptors of the epidermal growth factor receptor tyrosine kinase family (EGFR). This family consists of the EGF receptor (also known as Erb-B1), the Erb-B2 receptor, and its constituitively active oncoprotein mutant Neu, the Erb-B3 receptor and the Erb-B4 receptor. Additionally, other biological processes driven through members of the EGF family of receptors can also be treated by compounds of the invention described below. The EGFR has as its two most important ligands Epidermal Growth Factor (EGF) and Transforming Growth Factor alpha (TGFalpha). The receptors appear to have only minor functions in adult humans, but are apparently implicated in the disease process of a large portion of all cancers, especially colon and breast cancer. The closely related Erb-B2 Erb-B3 and Erb-B4 receptors have a family of Heregulins as their major ligands, and receptor overexpression and mutation have been unequivocally demonstrated as the major risk factor in poor prognosis breast cancer. Additionally, it has been demonstrated that all four of the members of this family of receptors can form heterodimeric signalling complexes with other members of the family, and that this can lead to synergistic transforming capacity if more than one member of the family is overexpressed in a malignancy. Overexpression of more than one family member has been shown to be relatively common in human malignancies.

Web site: http://www.delphion.com/details?pn=US06084095__

- **System and method for treating kidney diseases in diabetic and non-diabetic patients**

  Inventor(s): Aoki; Thomas T. (1021 El Sur Way, Sacramento, CA 95825)

  Assignee(s): none reported

  Patent Number: 6,613,342

  Date filed: June 15, 2001

  Abstract: The present invention is a system and method capable of improving the entire metabolic process and through its multiplicity of effects on neurovascular reactivity, intraglomerular pressure and hemodynamics, arresting the progression of overt diabetic nephropathy, improving intraglomerular hemodynamics, and thus arresting the progression of diabetic nephropathy and therefore reducing the risk of development of End Stage Renal Disease. The current system and method is for the treatment of **kidney disease** using insulin pulses to a patient utilizing Chronic Intermittent Intravenous Insulin Therapy to achieve the slowing, stopping or reversing of **kidney disease** in both diabetic and non-diabetic patient.

  Excerpt(s): This invention relates to the treatment of **kidney disease** in diabetic and non-diabetic patients. More specifically, the invention relates to a system and method for treating **kidney disease** in diabetic and non-diabetic patients with Chronic Intermittent Intravenous Insulin Therapy. Diabetic **kidney disease** (nephropathy) develops in 35 to 40% of patients with type 1 diabetes mellitus (DM) and in 10 to 60% of patients with

type 2 DM depending upon the ethnic pool being studied. It is the most common cause of End-Stage Renal Disease (ESRD) in the United States. Experts generally have assumed that diabetic nephropathy is the result of hyperglycemia, whether alone or in combination with other factors, such as hypertension and genetic susceptibility to **kidney disease.** Two major recent clinical trials involving patients with type 1 DM (Diabetes Control and Complication Trial [DCCT]) and type 2 DM (United Kingdom Prospective Diabetes Study [UKPDS]) have demonstrated that improved glycemic control reduces the onset and the progression of early diabetic nephropathy to overt nephropathy in patients recently diagnosed with diabetes mellitus (DM) thereby giving additional credence to the hypothesis that a lack of glycemic control is the primary cause. Both of theses studies used recently diagnosed patients some of whom, although well controlled, went on to develop **kidney disease.** Since the DCCT and UKPDS studies demonstrated that near normalization of blood glucose level did not always result in a delay of the onset or progression of diabetic nephropathy, the hypothesis that euglycemia is the means for addressing this disease, is made suspect. Once nephropathy has become clinically overt (that is, macroalbuminuria and decreased glomerular filtration rate are detected), the degree of glycemic control is shown to have lost its importance as a factor. This provides additional evidence to refute the claim that glycemic control is the primary factor to be addressed in **kidney disease,** and that other mechanisms have greater overall influence. Indeed, most patients with DM and proteinuria eventually will progress to ESRD or premature death from cardiovascular complications. In such patients, with no medical intervention, the glomerular filtration rate decreases an average of 1 ml/min per month, a deterioration that leads to ESRD in a mean period of 7 years. Once overt persistent proteinuria is established, no known strategy exists that can stop or reverse the progression to ESRD. Appropriate antihypertensive therapy has been shown to significantly reduce renal and possibly cardiovascular mortality in proteinuric type 1 DM patients, as well as retard the rate of decline of glomerular filtration rate in some patients with impaired renal function (Lewis A J et al, N Engl J Med 1993,329:1456-62). Thus, the standard of care for patients with diabetic nephropathy is intensive glycemic control and normalization of the blood pressure using primarily angiotensin converting enzyme inhibitors.

Web site: http://www.delphion.com/details?pn=US06613342__

- **Treatment of cystic disease with TNF-.alpha.**

  Inventor(s): Woo; David D. L. (Los Angeles, CA)

  Assignee(s): The Regents of the University of California (Oakland, CA)

  Patent Number: 5,750,495

  Date filed: March 26, 1996

  Abstract: A method for treating polycystic **kidney disease** in an individual in need thereof. This method includes identifying a mammal having a cystic disease and administering to the mammal a pharmacologically effective anti-cystic amount of TNF-.alpha. or an agent which stimulates TNF-.alpha. production in vivo. The agent is administered in a pharmacologically acceptable carrier, excipient or diluent.

  Excerpt(s): The present invention relates to treatment of cystic diseases. More specifically, the invention relates to treatment of polycystic **kidney disease** by administration of TNF-.alpha. or agents which stimulate production of TNF-.alpha. There are many human diseases which result in the formation of cysts which contain either semi-solid or fluid material. The contents of a cyst sometimes drive from normally

retained fluid (e.g. a sebaceous cyst can contain fluid from a blocked sebaceous gland) or from a parasitic infection. Benign cysts can occur in the ovary, spleen, lungs, kidney and liver, where they are often congenital. Some congenital cysts result from fetal malformations and developmental failure while others are directs results of a disease state. The polycystic kidney diseases (PKD) are a group of disorders characterized by the presence of a large number of fluid-filled cysts throughout grossly enlarged kidneys (Gabow et al., Diseases of the Kidney, Schrier et al. eds., 1992). In humans, PKDs can be inherited in autosomal dominant (ADPKD) or autosomal recessive (ARPKD) forms. ADPKD is the most common, dominantly-inherited **kidney disease** in humans, occurring at a frequency of about 1 in 800. ARPKD occurs at a frequency of about 1 in 10,000. Clinically, PKD represents a major cause of end-stage renal disease. Microdissection, histochemical and immunologic studies show that cysts in ARPKD kidneys arise from focal dilations of medullary collecting ducts (McDonald, Semin. Nephrol., 11:632-642, 1991). Mutations in at least three different loci have been associated with ADPKD in humans, including PKD1 on chromosome 16, PKD2 on chromosome 4, and the not yet mapped PKD3 (Reeders et al., Nature, 317:542-544, 1985; Kimberling et al., Genomics, 18:467-472, 1993; Daoust et al., Genomics, 25:733-736, 1995). The ARPKD mutation is on human chromosome 6 (Zerres et al., Nature Genet., 7:429-432, 1994). The molecular mechanisms leading to cyst enlargement and progressive loss of renal function in PKDs are not completely understood. Besides dialysis and transplantation, which are palliative, there are no preventive or curative treatment for PKDs.

Web site: http://www.delphion.com/details?pn=US05750495__

- **Treatment of polycystic kidney disease using vasopressin V.sub.2 receptor antagonists**

  Inventor(s): Gattone, II; Vincent H. (Overland Park, KS)

  Assignee(s): University of Kansas Medical Center (Kansas City, KS)

  Patent Number: 5,972,882

  Date filed: December 14, 1998

  Abstract: The present invention is directed to the novel treatment of ARPKD and ADPKD by administering a pharmacologically effective amount of a V.sub.2 receptor antagonist. Orally active V.sub.2 receptor antagonists such as OPC-31260, OPC-41061, SR121463A and VPA-985 are administered alone, or in combination to mammalian PKD subjects to reduce the cAMP generated by the increased expression of AVP-V.sub.2 receptor, AQP2 and AQP3, thereby reducing and/or preventing cyst enlargement.

  Excerpt(s): This invention relates to the treatment of polycystic **kidney disease** and, more particularly, to the use of vasopressin V.sub.2 receptor antagonists to reduce the cAMP generated by the increased expression of vasopressin V.sub.2 receptor, aquaporin-2 and aquaporin-3 after stimulation by arginine vasopressin. Polycystic **kidney disease** (PKD) is the most common inherited cause of end-stage renal disease afflicting an estimated 1 in 500 to 1 in 1000 persons. The two most prominent, inherited forms of PKD are autosomal dominant (ADPKD) generally characterized as being asymptomatic until adulthood, while autosomal recessive (ARPKD) is usually symptomatic in the perinatal or infantile period. The genes for ADPKD (i.e., ADPKD1 or polycystin, and ADPKD2) have been cloned and sequenced. The functional role of these unique and very different proteins in initiating cysts is not known. The chromosomal locations for the ARPKD gene in humans and the mouse model (the C57BL/6J-cpk/cpk

mouse) have been identified but neither gene has been cloned. Renal cysts are among the most common pathological structures observed in kidneys. Mangoo-Karim et al., Proc. Natl. Acad. Sci. USA, 86: 6007-11 (1989).sup.1 Cysts derive from nephron and collecting duct tissue and are isolated collections of urine-like fluid surrounded by a continuous epithelial layer. Cysts may be solitary and relatively innocent or so numerous (i.e., polycystic) that they compress and distort normal parenchyma and thereby cause renal insufficiency. Mangoo-Karim et al., supra.

Web site: http://www.delphion.com/details?pn=US05972882__

- **Use of.alpha.1.beta.1 integrin receptor inhibitors and TGF-.beta.1 inhibitors in the treatment of kidney disease**

  Inventor(s): Cosgrove; Dominic (Omaha, NE)

  Assignee(s): Boys Town National Research Hospital (Omaha, NE)

  Patent Number: 6,492,325

  Date filed: April 15, 1999

  Abstract: The present invention provides methods for treating (i.e., delaying the onset of, slowing the progression of, and/or reversing) kidney disorders (e.g., renal glomerulonephritis and/or renal fibrosis). Certain of these methods involve administering an.alpha.1.beta.1 integrin receptor inhibitor optionally in combination with a TGF-.beta.1 inhibitor. The present invention also provides a mouse model for **kidney disease** wherein the mouse does not express a normal collagen type 4 composition in the GBM (i.e., it does not incorporate collagen.alpha.3(IV),.alpha.4(IV), and.alpha.5(IV) chains into its glomerular basement membrane) and does not express the.alpha.1.beta.1 integrin receptor.

  Excerpt(s): This invention relates to the field of **kidney disease** (i.e., kidney disorder) characterized by glomerulonephritis and/or fibrosis. In particular, this invention relates to the use of.alpha.1.beta.1 integrin receptor inhibitors in kidney disorders. Further, this invention relates to the use of.alpha.1.beta.1 integrin inhibitors in combination with TGF-.beta.1 inhibitors in kidney disorders. In the United States, approximately 12,000 people currently live with Alport syndrome. This inherited disorder results in progressive renal disease that is only treatable by dialysis and kidney transplant. Transplanted kidneys are usually rejected. Thus, alternative treatments are needed. However, there is currently no treatment that addresses the mechanism of the disease onset or progression. Thus, what is needed is a treatment method that attacks the mechanism of disease onset and/or progression, one that could substantially slow disease conditions, such as renal glomerulonephritis and renal fibrosis. A number of kidney diseases are associated with alterations in matrix homeostasis, where the delicate balance of synthesis and turnover of structural molecules is interrupted. As one example, Alport syndrome is a disease resulting in progressive renal failure and is associated with sensorineural hearing loss. Male carriers are most affected and ultrastructural studies reveal abnormalities in the glomerular basement membrane (GBM) of affected individuals. About one in 20,000 people have Alport syndrome, making the disease one of the more prevalent known genetic disorders. See, for example, Atkin et al., "Alport Syndrome" In R. W. Schrier & C. W. Gottschalk (Eds.), Diseases of the Kidney, 4th ed., Chap. 19, Little Brown, Boston, pp. 617-641, 1988. X-linked Alport syndrome is caused by any of a series of mutations in the collagen 4A5 gene (Barker et al., Science, 248:1224-1227, 1990). At least 60 different mutations in the gene have been identified. The autosomal form of Alport syndrome displays the same

range of phenotypes as the X-linked form and results from mutations in either basement membrane collagen gene 4A3 (COL4A3) or 4A4 (COL4A4). See, for example, Lemmink et al., Hum. Mol. Gen., 3:1269-1273, 1994, and Mochizuki et al., Nature Genet., 8:77-81, 1994. Other diseases of the basement membrane include Goodpasture syndrome, which is due to an acute autoimmune response directed against an epitope on the NCl domain of collagen 4A3 (Hudson et al., Kidney Int., 43:135-139, 1993), and diffuse leiomyomatosis, a benign smooth muscle tumor that is associated with a deletion of both collagen 4A5 and 4A6 (Zhou et al., Science, 261:1167-1169, 1993).

Web site: http://www.delphion.com/details?pn=US06492325__

- **Use of IGF-I for the treatment of kidney disorders**

  Inventor(s): Acott; Philip D. (Halifax, CA), Crocker; John F. S. (Halifax, CA)

  Assignee(s): Dalhousie University (Halifax, CA)

  Patent Number: 5,985,830

  Date filed: September 16, 1997

  Abstract: In accordance with the present invention, there are provided methods for the treatment of polycystic **kidney disease** and related indications in mammals, employing IGF-I as the active agent. In accordance with another embodiment of the present invention, it has been discovered that IGF-I is an effective agent for the treatment of renal dysplasias and/or renal hypoplasias in mammals. In accordance with yet another embodiment of the present invention, it has been discovered that IGF-I is an effective agent for enhancing glomerular development in mammals. In accordance with still another embodiment of the present invention, it has been discovered that IGF-I is an effective agent for enhancing kidney development in mammals suffering from chronic organ injury.

  Excerpt(s): The present invention relates to methods for the treatment of polycystic **kidney disease** in mammals. In another aspect, the present invention relates to methods for the treatment of renal dysplasias and/or renal hypoplasias in mammals. In yet another aspect, the present invention relates to methods to enhance glomerular development in mammals. In still another aspect, the present invention relates to methods to enhance kidney development in mammals suffering from chronic organ injury. In a further aspect, the present invention relates to methods to protect subjects from the ongoing toxicity of treatment with steroid hormones. In a still further aspect, the present invention relates to methods to maintain substantially normal growth in neonates and pre-pubescent mammals exposed to high dose steroid hormone therapy. Polycystic **kidney disease** is a heterogenous group of disorders characterized by large kidneys with epithelial lined cysts along the nephron collecting ducts of the affected kidneys. In all types of cystic **kidney disease,** the enlargement of the cyst wall is associated with hyperplasia of renal epithelium. There are several examples of genetic predisposition to cystic disease, with the most common forms of human polycystic **kidney disease** (PKD) being genetically transmitted as either an autosomal dominant trait or an autosomal recessive trait. There are also several forms of acquired polycystic **kidney disease.** Acquired lesions are caused by broad categories of agents, such as teratogens (e.g., diphenylamine and phthalates), agents affecting metanephric development (e.g., steroid hormones such as glucocorticoids), and as a consequence of loss of renal mass (as seen in end-stage renal disease). Even in kindreds with a defined genetic mutation, there is broad expression of the clinical phenotype. An example of this is a family with autosomal recessive PKD in several siblings, where the onset of renal

failure was variable in the child and adolescent years. It is also well established that autosomal dominant PKD is asymptomatic in half of the kindred who are genetically affected, while approximately 1/6 go to renal failure. Moreover, the genetic trait does not discriminate the phenotypic variation of gender. The observation that the genetics are only one part of the clinical phenotype of PKD has created interest in looking at the pathophysiology of cystic disease and progression in the hope of finding modifying agents. Currently, however, there is no effective treatment for Polycystic **Kidney Disease** (PKD), one of the three leading causes of end stage renal failure in humans (Canadian Organ Replacement Register; p. 95 [1990]). Although PKD simulates Mendelian inheritance, there is evidence that phenotypic expression of PKD involves genetic heterogeneity and multifactorial inheritance, including nongenetic factors.

Web site: http://www.delphion.com/details?pn=US05985830__

- **Use of peptides inhibitory for thrombospondin dependent TGF-.beta. activation in the treatment of kidney disease**

  Inventor(s): Hugo; Christian (Weideu/Opt, DE), Krutzsch; Henry C. (Bethesda, MD), Murphy-Ullrich; Joanne E. (Birmingham, AL), Ribeiro; Solange M. F. (Birmingham, AL), Roberts; David D. (Bethesda, MD)

  Assignee(s): The UAB Research Foundation (Birmingham, AL)

  Patent Number: 6,458,767

  Date filed: May 28, 1999

  Abstract: The present invention provides a method of treating kidney or renal diseases/conditions in a subject by administering to the subject a pharmaceutically effective amount of a purified LAP peptide, a TSP-1 type 1 repeat peptide, or a fragment thereof to interfere with the activation process of TGF-.beta. by thrombospondin-1 to reduce and/or prevent renal damage. The present invention further provides a method of improving renal function in a subject having impaired renal function by administering to the subject a pharmaceutically effective amount of a purified LAP peptide, a TSP-1 type 1 repeat peptide, or a fragment thereof.

  Excerpt(s): The present invention generally relates to a method of regulating transforming growth factor TGF-.beta. (TGF-.beta.) activity. More particularly, the present invention relates to a method of interfering with the activation of TGF-.beta. by thrombospondin through the administration of peptides in order to treat kidney diseases and/or conditions. Extracellular matrix accumulation is one of the hallmarks of inflammatory glomerular disease as a major cause of end-stage renal disease in man. Mesangial proliferative glomerulonephritis, the most common type of glomerulonephritis in the Western World (D'Amico (1987) QJM 245, 709-727), is characterized by mesangial cell (MC) proliferation, activation, and extracellular matrix expansion (Johnson (1994) Kidney Int. 45 (6), 1769-82). In up to 50% of the patients with mesangial proliferative glomerulonephritis, the disease process eventually progresses to end-stage renal disease, since specific treatment is still lacking (Galla (1995) Kidney Int. 47, 377-387). Typical features of human mesangial proliferative glomerulonephritis are mimicked by an experimental model in the rat, induced by an antibody against the Thy1-antigen on MC ((Johnson (1994) Kidney Int. 45 (6), 1769-82). In this model, a single injection of anti-thymocyte antibody results in an acute, complement-dependent MC injury (days zero to two) with proteinuria, followed by a FGF-2- and PDGF-dependent MC proliferative response that is accompanied by a TGF-.beta.-dependent overproduction of extracellular matrix proteins (days three to ten) (Johnson (1994)

Kidney Int. 45 (6), 1769-82). The role of TGF-.beta. as a major profibrotic cytokine in the anti-Thy1 model has been well established (Border et al. (1994) N. Engl. J. Med. 331, 1286-1292). It has been demonstrated that TGF-.beta.1 mRNA and protein are increased in the anti-Thy1 model (Okuda et al. (1990) J. Clin. Invest. 86, 453-462) and that blocking TGF-.beta.1 by injections with a polyclonal anti-TGF-.beta.1 antibody markedly reduced extracellular matrix accumulation (Border et al. (1990) Nature 346, 371-374). Injections with the proteoglycan decorin, a TGF-.beta.1, -2, and -3 binding protein, also suppressed TGF-.beta.-dependent alterations such as extracellular matrix accumulation in the anti-Thy1 model (Border et al. (1992) Nature 360, 361-364). The results of these studies by Border and colleagues were confirmed by studies using gene transfer techniques in the anti-Thy1 model. Transfer of antisense oligonucleotides against the TGF-.beta.1 mRNA into the rat kidney suppressed upregulation of glomerular TGF-.beta.1 mRNA and protein as well as extracellular matrix accumulation (Akaki et al. (1996) Kidney Int. 50, 148-155). Transfer of decorin cDNA into rat skeletal muscle increased the amount of decorin in skeletal muscle and in the kidney, and again ameliorated glomerular disease by decreasing matrix formation (Isaka et al. (1996) Nat. Med. 2, 418-423). In contrast, mice transgenic for an active form of TGF-.beta.1 exhibit elevated plasma levels of TGF-.beta.1 and develop progressive renal disease characterized by MC matrix accumulation, interstitial fibrosis, and proteinuria (Kopp et al. (1996) Lab. Invest. 74, 991-1003). Transfer of the TGF-.beta.1 gene into glomeruli of normal rats caused an increase in glomerular TGF-.beta.1 protein that was linked to extracellular matrix formation (Isaka et al (1993) J. Clin. Invest. 92, 2597-2601). The potential importance of TGF-.beta. in mediating fibrosis also in human **kidney disease** has been supported by the widespread link of TGF-.beta. upregulation and extracellular matrix excess in many different types of human **kidney disease** (Border et al. (1994) N. Engl. J. Med. 331, 1286-1292).

Web site: http://www.delphion.com/details?pn=US06458767__

Patent Applications on Kidney Disease

As of December 2000, U.S. patent applications are open to public viewing.[10] Applications are patent requests which have yet to be granted. (The process to achieve a patent can take several years.) The following patent applications have been filed since December 2000 relating to kidney disease:

- **3-cyanoquinolines, 3-cyano-1,6-naphthyridines, and 3-cyano-1,7-naphthyridi- nes as protein kinase inhibitors**

  Inventor(s): Berger, Dan Maarten; (New City, NY), Boschelli, Diane Harris; (New City, NY), Boschelli, Frank Charles; (New City, NY), Demorin, Frenel Fils; (Thousand Oaks, CA), Overbeek-Klumpers, Elsebe Geraldine; (Bk Bergentheim, NL), Powell, Dennis William; (Cortlandt Manor, NY), Tsou, Hwei-Ru; (New City, NY), Wang, Yanong; (Nanuet, NY), Wissner, Allan; (Ardsley, NY), Wu, Biqi; (Nanuet, NY), Yamashita, Ayako; (Englewood, NJ), Ye, Fei; (Nanuet, NY), Zhang, Nan; (Bayside, NY)

  Correspondence: Egon E. Berg; American Home Products Corporation; Patent Law Department; Five Giralda Farms; Madison; NJ; 07940; US

  Patent Application Number: 20020026052

  Date filed: March 28, 2001

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

Abstract: This invention provides compounds of Formula (I), having the structure 1where T, Z, X, A, R.sup.1, R.sup.2a, R.sup.2b, R.sup.2c, R.sup.3, R.sup.4, and n are defined herein, or a pharmaceutically acceptable salt thereof which are useful as antineoplastic agents and in the treatment of osteoporosis and polycystic **kidney disease.**

Excerpt(s): This application claims benefit of U.S. Provisional Application No. 60/219,322 which was converted from U.S. patent application Ser. No. 09/535,843 filed Mar. 28, 2000 pursuant to a petition filed under 37 C.F.R. 1.53 (c) (2) filed Aug. 2, 2000. This invention relates to 3-cyanoquinoline, 3-cyano-1,6-naphthyiidi- ne and 3-cyano-1,7-naphthyiidine containing compounds as well as their pharmaceutically acceptable salts. The compounds of the present invention inhibit the activity of protein kinases that are required for cell growth and differentiation. The compounds of this invention are therefore useful for the treatment of certain diseases that result from activity of these protein kinases. The compounds of this invention are anti-cancer agents and are useful for the treatment of cancer in mammals. In addition, the compounds of this invention are useful for the treatment of polycystic **kidney disease** in mammals. The compounds of this invention may also be used in the treatment of osteoporosis. This invention also relates to the manufacture of said compounds, their use for the treatment of cancer, polycystic **kidney disease** and osteoporosis, and the pharmaceutical preparations containing them. Protein kinases are enzymes that catalyze the transfer of a phosphate group from ATP to an amino acid residue, such as tyrosine, seline, threonine, or histidine on a protein. Regulation of these protein kinases is essential for the control of a wide variety of cellular events including proliferation and migration. Specific protein kinases have been implicated in diverse conditions including cancer [Traxler, P. M., Exp. Opin. Ther. Patents, 8, 1599 (1998); Bridges, A. J., Emerging Drugs, 3, 279 (1998)], restenosis [Mattsson, E., Trends Cardiovas. Med. 5, 200 (1995); Shaw, Trends Pharniacol. Sci. 16, 401 (1995)], atherosclerosis [Raines, E. W., Bioessays, 18, 271 (1996)], angiogenesis [Shawver, L. K., Drug Discovery Today, 2, 50 (1997); Folkman, J., Nature Medicine, 1, 27 (1995)] and osteoporosis [Boyce, J. Clin. Invest., 90, 1622 (1992)].

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

- **Compositions and methods for genetic analysis of polycystic kidney disease**

  Inventor(s): Allen, Susan Kimberly; (Worcester, MA), Curran, John A.; (Worcester, MA), Flynn, Kerry Ellen; (Grafton, MA), Garces, Jorge A.; (Dudley, MA), Hennigan, Aidan Noel; (Millbury, MA), Jones, Jeffrey George; (Wilbraham, MA), Palatucci, Christopher M.; (Shrewsbury, MA), Robichaud, Normand J.; (Leominster, MA), Wang, Jing; (Worcester, MA)

  Correspondence: Palmer & Dodge, Llp; Kathleen M. Williams; 111 Huntington Avenue; Boston; MA; 02199; US

  Patent Application Number: 20030152936

  Date filed: February 26, 2002

  Abstract: The subject invention relates to methods for detection of mutations in a PKD gene using DHPLC. The invention includes the following aspects: identification of PKD unique sites; design of PKD-specific primers; amplification of PKD-specific products; and analysis of PCR amplified products by DHPLC. The invention further relates to compositions such as identified unique sites and PKD-specific primers, and kits for performing the methods of the invention.

Excerpt(s): The invention relates to a genetic testing method for identifying alterations or the absence of such alterations in a gene associated with Autosomal Dominant Polycystic **Kidney Disease.** Autosomal dominant polycystic **kidney disease** (ADPKD) is an exceptionally common hereditary nephropathology with an incidence of about 1 in 800 live births. The disease is progressive, phenotypically characterized by bilaterally enlarged polycystic kidneys, and typically resulting in end-stage renal disease (ESRD) by the age of 65 years. The more common complications include hypertension, macrohaematuria, urinary-tract infection, cardiac-valve abnormalities, and hernia of the anterior abdominal wall. Cyst formation is also commonly observed in the liver, although the occurrence is not associated with functional impairment of the organ. Although not as frequently reported, additional extrarenal manifestations include pancreatic cysts, connective tissue abnormalities, and cerebral-artery aneurysms. The typical age of onset is in middle life, but the range is from infancy to 80 years. The clinical presentation of ADPKD differs between and within families as partly explained by the genetically heterogeneous nature of the disorder. Mutations in two genes, PKD-1 and PKD-2, account for nearly all cases of ADPKD (e.g., for reviews, see Arnaout, 2001, Annu Rev. Med. 52:93-123; Koptides and Deltas, 2000, Hum. Genet. 107:115-126). PKD-1 and PKD-2 encode integral membrane proteins whose functions have not been fully elucidated. The major gene responsible for ADPKD, PKD-1, has been fully characterized and shown to encode an integral membrane protein, polycystin 1, which is thought to be involved in cell-cell and cell-matrix interaction. PKD-2 gene encodes polycystin-2 which is a predicted integral membrane protein with non-selective cation channel activity. Based on sequence homology with the alpha 1 subunit component of voltage-activated calcium channels, it has been postulated that polycystin-2 may play a role in ion channeling. The C-terminal cytoplasmic tails of polycystin-1 and polycystin-2 have been shown to interact using in vitro binding assays and in a directed two-hybrid interaction. The interaction occurs via a coiled-coil domain in PKD-1 and a region near R872 in PKD-2. Although the biological relevance of the interaction between the polycystins is not yet understood, it does suggest that PKD-1 and PKD-2 are likely to function along a common pathway.

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

- **Method for kidney disease detection by protein profiling**

  Inventor(s): Comper, Wayne D.; (Victoria, AU)

  Correspondence: Mcdermott, Will & Emery; 600 13th Street, N.W.; Washington; DC; 20005-3096; US

  Patent Application Number: 20030003588

  Date filed: October 26, 2001

  Abstract: The invention provides a method of generating and analyzing a urinary protein fragmentation profile, in terms of the size, and sequence of particular fragments derived from intact filtered proteins together with the position where enzymes scission occurs along the protein polypeptide chain is characteristic of the diseased state of the kidney.With the recognition that filtered proteins are degraded during renal passage, the methods described in this application will be able to detect protein fragments derived from proteins generated by non-renal disease. Non-renal disease such as cancers may generate increased levels of proteins into the circulation. The urinary analysis of these filtered proteins would currently not detect the intact form of these proteins. Therefore, a method as described to detect and analyze fragments resulting

from degradation during renal passage that will be able to detect the seriousness of the disease.

Excerpt(s): This application claims priority to U.S. Provisional Application Serial No. 60/301,251, filed Jun. 28, 2001. The invention relates to improved methods of detecting an early stage of renal disease and/or renal complications of a disease, particularly diabetes. The appearance of excess protein such as albumin in the urine is indicative of **kidney disease.** Diabetic nephropathy is such a disease.

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

- **Method for the regioselective preparation of substituted benzo[g]quinoline3-carbonitriles and benzo[g]quinazolines**

  Inventor(s): Berger, Dan Maarten; (New City, NY), Birnberg, Gary Harold; (Tuxedo Park, NY), Wang, Yanong Daniel; (Nanuet, NY)

  Correspondence: Wyeth; Five Giralda Farms; Madison; NJ; 07940; US

  Patent Application Number: 20020091273

  Date filed: January 11, 2002

  Excerpt(s): This application claims priority from copending provisional application(s) serial No. 60/259,190 filed on Dec. 29, 2000, the entire disclosure of which is hereby incorporated by reference. This invention relates to a method for the regioselective synthesis of 4,6,7,8-substituted benzo[g]quinoline-3-carbonitriles and 4,6,7,8-substituted benzo[g]quinazolines as well as intermediates thereof. The compounds derived from this invention are useful for the treatment of a variety of diseases that are a result of deregulation of these PTK's, and more specifically, are anti-cancer agents and are useful for the treatment of cancer in mammals. In addition, the compounds derived from this invention are useful for the treatment of polycystic **kidney disease** in mammals. Certain 4-anilino-benzo[g]quinoline-3-carbonitriles as protein kinase inhibitors are disclosed in PCT patent application WO0147892.

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

- **Method to follow progression of kidney disease**

  Inventor(s): Dunn, Stephen R.; (Philadelphia, PA), Falkner, Bonita; (Philadelphia, PA), McGowan, Tracy A.; (Philadelphia, PA), Sharma, Kumar; (Berwyn, PA)

  Correspondence: Thomas Jefferson University; Intellectual Property Division; 1020 Walnut Street; Suite 620; Philadelphia; PA; 19107; US

  Patent Application Number: 20030059956

  Date filed: May 3, 2002

  Abstract: The present invention relates to methods of measuring urinary TGF-.beta. levels to monitor disease progression in patients having chronic fibrotic diseases or kidney diseases, more particularly, methods of preparing urine specimens for measuring urinary TGF-.beta. levels in patients having chronic fibrotic diseases or kidney diseases.

  Excerpt(s): This application claims priority under 35 U.S.C.sctn.119 based upon U.S. Provisional Patent Application No. 60/288,307 filed on May 3, 2001. The instant

invention is generally related to urology, more particularly, methods of preparing urine specimens for use in measuring TGF-.beta. levels. ACE means "angiotensin-converting enzyme".

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

- **Methods and compositions for analysis of urine samples in the diagnosis and treatment of kidney diseases**

  Inventor(s): Kurnit, David M.; (Ann Arbor, MI)

  Correspondence: Rader, Fishman & Grauer Pllc; 39533 Woodward Avenue; Suite 140; Bloomfield Hills; MI; 48304-0610; US

  Patent Application Number: 20030198959

  Date filed: March 28, 2002

  Abstract: The invention comprises novel compositions, systems, and methods for the analysis of biological samples, such as urine samples, in order to diagnose and treat **kidney disease,** including without limitation, glomerulonephritis, nephrotic syndrome, diabetes, lupus, hypertension, acute tubular necrosis, obstructive disorders of the urinary tract, renal cancers and other diseases or syndromes. In preferred embodiments, the invention comprises the identification of particular genes expressed only in cells of particular clinical or scientific interest in the urinary tract, such as podocytes or proximal tubule cells. Thus, the invention enables non-invasive, rapid and accurate analysis of kidney and urinary tract status and function in many medical diseases and disorders.

  Excerpt(s): The invention relates to the analysis of biological samples in the diagnosis and treatment of **kidney disease.** Specifically, the invention relates to the analysis of urine samples to diagnose as well as to monitor the progress of treatment of kidney diseases and disorders associated with a variety of conditions including, but not limited to, glomerulonephritis, nephrotic syndrome, diabetes, lupus, hypertension, acute tubular necrosis (ATN), renal obstructive disorders, renal cancers and other diseases or syndromes. Physicians who treat patients often require analyses of kidney status and function. For diseases such as glomerular disorders, this is currently accomplished by detection of protein (albumin) present in the urine, that is, by assaying the amount of protein spilled into the urine from the kidney. However, this method can be insensitive and untimely because much kidney function must be lost before an abnormal test result appears. It may also be inaccurate because there are many non-specific causes of protein in the urine, and testing for elevated albuminuria may be falsely positive in many subjects. Moreover, for some kidney disorders, such as proximal tubule disorders, sensitive urine-based tests are generally not available. The alternative for analysis is a kidney biopsy that is expensive, invasive and associated with a finite morbidity due to the risks of bleeding and infection. The only currently available urine-based test for monitoring podocyte disease directly, which is used only experimentally, is an antibody test for podocytes excreted in the urine. However, this test is not as sensitive as the method we present, as it only becomes abnormal when albumin is present in the urine. Thus, there is need for a specific, generally available test that shows positive association with renal dysfunction earlier in the course of **kidney disease,** preferably close to the outset.

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

- **Methods for production of growth-promoting proteins and peptides for kidney epithelial cells**

  Inventor(s): Toback, F. Gary; (Chicago, IL), Walsh-Reitz, Margaret M.; (River Forest, IL)

  Correspondence: Barnes & Thornburg; 2600 Chase Plaza; 10 South Lasalle Street; Chicago; IL; 60603; US

  Patent Application Number: 20030176340

  Date filed: November 22, 2002

  Abstract: Novel growth peptides derived from protein factors having molecular weights of about 22 and 45 kDa stimulate mitogenic activity of epithelial, but not fibroblastic cells, in particular, kidney epithelial cells. A source of the factors is scrape-wounded kidney epithelial cells in culture. Synthetic peptides having sixteen amino acids or less, in particular a hexapeptide, YPQGNH (SEQ ID NO: 2) maintain the mitogenic activity. The peptide AQPYPQGNHEASYG (14-Ser) (SEQ ID NO: 15) is effective in reversing acute renal failure in animals. The growth-promoting characteristics of the 22 and 45 kDa proteins and the peptides are useful in treating and diagnosing patients with **kidney disease.** Nucleotide sequences that encode the factor are useful to develop probes to locate similar factors, to identify genetic disorders involving the factor, and to produce the factor by genetic recombinant methods. The nucleotide sequences and fragments thereof, are also useful for diagnosis and treatment of kidney disorders.

  Excerpt(s): This application claims priority to U.S. Ser. No. 08/974,775 filed Nov. 20, 1997 now U.S. Pat. No. 6,096,706 issued Aug. 1, 2002 and U.S. Ser. No. 09/590,864 for which claims have been allowed and the issue fee paid. Novel growth peptides derived from protein factors having molecular weights of about 22 and 45 kDa stimulate mitogenic activity of epithelial, but not fibroblastic cells, in particular, kidney epithelial cells. Acute renal failure is a serious disease associated with high mortality for which no "real" treatment currently exists. Acute renal failure is defined as the abrupt disruption of previously normal kidney function. It is caused by a wide variety of mechanisms including circulatory failure (shock), vascular blockade, glomerulonephritis, and obstruction to urine flow. In addition it can occur following surgery, trauma, sepsis, or with certain medications, particularly antibiotics and anticancer agents.

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

- **Methods of kidney transplantation utilizing developing nephric tissue**

  Inventor(s): Dekel, Benjamin; (Tel-Aviv, IL), Reisner, Yair; (Tel Aviv, IL)

  Correspondence: G.E. Ehrlich (1995) LTD.; C/o Anthony Castorina; Suite 207; 2001 Jefferson Davis Highway; Arlington; VA; 22202; US

  Patent Application Number: 20030096016

  Date filed: April 10, 2002

  Abstract: A method of treating a **kidney disease** in a subject is disclosed. The method is effected by transplanting into the subject a graft of nephric tissue at a predetermined developmental stage thereby treating the **kidney disease** in the subject.

  Excerpt(s): The present invention relates to methods of treating kidney diseases. More particularly, the present invention relates to methods of treating **kidney disease** via transplantation of developing human or porcine nephric tissues. Treatment of **kidney disease** via MHC haplotype-matched allogeneic kidney transplantation is a widely

practiced, and often life-saving, therapeutic modality which, nevertheless, suffers from serious limitations. The rarity of available donor organs and the necessity to obtain organs from histocompatible and morphologically compatible donors, which are often poorly represented in the donor pool, results in numerous renal failure related deaths each year.

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

- **Nephrin gene and protein**

  Inventor(s): Kestila, Marjo; (Oula, FI), Lenkkeri, Ulla; (Oulu, FI), Mannikko, Minna; (Philadelphia, PA), Tryggvason, Karl; (Djursholm, SE)

  Correspondence: Richard J. Minnich; Fay, Sharpe, Fagan, Minnich & Mckee; Suite 700; 1100 Superior Avenue; Cleveland; OH; 44114-2518; US

  Patent Application Number: 20020004589

  Date filed: January 12, 2001

  Abstract: The present invention provides for compositions and methods for detecting susceptibility for basement membrane disease, in particular Congenital nephrotic syndromes of the Finnish type. The present invention provides for nucleic acids and protein for use in methods and compositions for the diagnosis of disease and identification of small molecule therapeutics for treatment of such disease, in particular of proteinuria associated with **kidney disease.**

  Excerpt(s): Congenital nephrotic syndrome of the Finnish type (CNF, NPHS1, MIM 256300) is an autosomal recessive disorder, and a distinct entity among congenital nephrotic syndromes. It is characterized by massive proteinuria at the fetal stage and nephrosis at birth. Importantly, NPHS1 appears to solely affect the kidney and, therefore, it provides a unique model for studies on the glomerular filtration barrier. The primary barrier for ultrafiltration of plasma in renal glomeruli comprises three layers; a fenestrated endothelium, a 300-350 nm thick glomerular basement membrane (GBM), and slit pores, i.e. diaphragms located between the foot processes of the epithelial cells. This barrier is a highly sophisticated size-selective molecular sieve whose molecular mechanisms of function are still largely unclarified. It is anticipated that the GBM, a tightly cross-linked meshwork of type IV collagen, laminin, nidogen and proteoglycans, contains pores that restrict the penetration of large proteins and cells, and, additionally, it has been hypothesized that anionic heparan sulfate proteoglycan components contribute to an electric barrier for macromolecules (Kasinath and Kanwar, 1993). The glomerular filter is affected in a large number of acquired and inherited diseases resulting in extensive leakage of plasma albumin and larger proteins leading to nephrotic syndrome and end stage renal disease. Understanding of the molecular mechanisms of the glomerular filtration process and its pathology is of fundamental importance for clinical medicine, which, in turn, may facilitate novel developments for diagnosis and treatment of complications in primary and secondary diseases of the kidney. Genetic diseases with defects in the filtration barrier as major symptoms can serve as models for providing such knowledge. Congenital nephrotic syndromes (NPHS) form a heterogenous group of diseases characterized by massive proteinuria at or shortly after birth (Rapola et al., 1992). Nephrotic syndrome can be primary, acquired, or a part of other syndromes. Congenital nephrotic syndrome of the Finnish type (CNF, NPHS1) is a distinct entity among NPHS. It is an autosomal recessive disorder with an incidence of 1:10,000 births in Finland, but considerably less in other countries (Norio, 1966; Huttunen, 1976). The disease manifests itself already at the fetal stage with heavy

proteinuria in utero, demonstrating early lesions of the glomerular filtration barrier. The pathogenesis of NPHS1 has remained obscure. There are no pathognomonic pathologic features, the most typical histological finding of NPHS1 kidneys being dilation of the proximal tubuli (Huttunen et al. 1980). The kidneys are also large and have been found to contain a higher amount of nephrons than age-matched controls (Tryggvason and Kouvalainen, 1975). Electron microscopy reveals no abnormal features of the GBM itself, although there is a loss of foot processes of the glomerular epithelial cells, a finding characteristic for nephrotic syndromes of any cause. Analyses of GBM proteins, such as type IV collagen, laminin, and heparan sulfate proteoglycan have not revealed abnormal findings in NPHS1 (e.g. see Ljungberg et al. 1993, Kestil et al. 1994a). NPHS1 is a progressive disease, usually leading to death during the first two years of life, the only life-saving treatment being kidney transplantation (Holmberg et al. 1995). Importantly, most transplanted patients have, thus far, not developed extrarenal complications, suggesting that the mutated gene product is highly specific for kidney development and/or glomerular filtration function. However, about 20% of the patients have developed post-transplantation nephrosis the cause of which is unknown (Laine et al., 1993; Holmberg et al., 1995).

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

- **Nitrosated and nitrosylated taxanes, compositions and methods of use**

  Inventor(s): Garvey, David S.; (Dover, MA), Letts, L. Gordon; (Dover, MA), Lin, Chia-En; (Burlington, MA), Richardson, Stewart K.; (Tolland, CT), Wang, Tiansheng; (Concord, MA)

  Correspondence: Edward D Grieff; Hale & Dorr Llp; 1455 Pennsylvania Ave, NW; Washington; DC; 20004; US

  Patent Application Number: 20020010146

  Date filed: June 22, 2001

  Abstract: The present invention describes novel nitrosated and/or nitrosylated taxanes, and novel compositions comprising at least one nitrosated and/or nitrosylated taxane, and, optionally, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one therapeutic agent. The present invention also provides novel compositions comprising at least one taxane and at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one therapeutic agent. The compounds and compositions of the present invention can also be bound to a matrix. The present invention also provides methods for treating or preventing cardiovascular diseases and disorders, autoimmune diseases, pathological conditions resulting from abnormal cell proliferation, polycystic **kidney disease,** inflammatory disease, preserving organs and/or tissues or to inhibit wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis, by administering nitrosated and/or nitrosylated taxane or parent taxanes in combination with nitric oxide donors that are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiological conditions.

  Excerpt(s): This application claims priority to U.S. Provisional Application No. 60/213,294 filed Jun. 22, 2000 and U.S. Provisional Application No. 60/226,090 filed Aug. 18, 2000. Endothelium-derived relaxing factor (EDRF) is a vascular relaxing factor

secreted by the endothelium and is important in the control of vascular tone, blood pressure, inhibition of platelet aggregation, inhibition of platelet adhesion, inhibition of mitogenesis, inhibition of proliferation of cultured vascular smooth muscle, inhibition of leukocyte adherence and prevention of thrombosis. EDRF has been identified as nitric oxide (NO) or a closely related derivative thereof (Palmer et al, Nature, 327:524-526 (1987); Ignarro et al, Proc. Natl. Acad. Sci. USA, 84:9265-9269 (1987)).

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

- **Novel compounds for the management of aging-related and diabetic vascular complications, process for their preparation and therapeutic uses thereof**

  Inventor(s): Sankaranarayanan, Alangudi; (Ahmedabad, IN)

  Correspondence: Sughrue, Mion, Zinn, Macpeak & Seas, Pllc; 2100 Pennsylvania Avenue, N.W.; Washington; DC; 20037-3202; US

  Patent Application Number: 20010018524

  Date filed: March 9, 2001

  Abstract: Novel compounds of the pyridinium series useful for the management of diabetes and aging-related vascular complications, including **kidney disease,** nerve damage, atherosclerosis, retinopathy, dermatological disorders and discoloration of teeth, by breaking preformed AGE, of the general formula I, or pharmaceutically acceptable salts thereof, 1wherein, R.sub.1, R.sub.2, R.sub.3, X and m are as defined in the specification. Also disclosed is a method for preparation of the compounds of general formula (I) and pharmaceutical composition containing one or more compounds as defined above as active ingredients. Also disclosed is a method of treatment of a diabetic patient by administering the compounds as defined above, either singly or in combination with drugs for antidiabetic therapy.

  Excerpt(s): This is a continuation-in-part application of application Ser. No. 09/598,410 filed Jun. 21,2000, which is a continuation-in-part application of International application PCT/1B99/01683 filed on Oct., 15, 1999, the disclosures of which are incorporated herein by reference. The present invention relates to a new class of compounds of pyridinium series and to their use in treatment of diabetes and related illnesses. More particularly the invention relates to compounds of this series, methods for their preparation, pharmaceutical composition containing these compounds and their use in the treatment of complications of diabetes mellitus. The compounds of this series exhibit AGE breaking activity, which is essential for the treatment of diabetic and aging-related complications including **kidney disease,** nerve damage, atherosclerosis, retinopathy and dermatological conditions. The invention also extends to the method of reversing the discoloration of teeth resulting from nonenzymatic browning in the oral cavity which comprises administration of an amount effective to reverse pre-formed advanced glycosylation crosslinks. 2. Description of the Related Art.

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

- **Novel compounds for the management of aging-related and diabetic vascular complications, process for their preparation and therapeutic uses thereof**

  Inventor(s): Sankaranarayanan, Alangudi; (Ahmedabad, IN)

  Correspondence: Sughrue Mion, Pllc; 2100 Pennsylvania Avenue, NW; Washington; DC; 20037-3213; US

  Patent Application Number: 20030092744

  Date filed: August 9, 2002

  Abstract: The invention discloses novel compounds of the pyridinium series useful for the management of diabetes and aging-related vascular complications, including **kidney disease,** nerve damage, atherosclerosis, retinopathy, dermatological disorders and discoloration of teeth, by breaking preformed AGE, of the general formula I, or pharmaceutically acceptable salts thereof, 1wherein, R.sub.1, R.sub.2, R.sub.3, X and m are as defined in the specification.The invention also discloses, method for preparation of the novel compounds of the series and pharmaceutical composition having one or more compounds as defined above as active ingredients.The invention further discloses a method of treatment of a diabetic patient by administering the compounds as defined above, either singly or in combination with drugs for antidiabetic therapy.

  Excerpt(s): This is a continuation-in-part application of International Application No. PCT/IB99/01683 filed on Oct., 15, 1999, the disclosure of which is incorporated herein by reference. The present invention relates to a new class of compounds of pyridinium series and to their use in treatment of diabetes and related illnesses. More particularly the invention relates to compounds of this series, methods for their preparation, pharmaceutical composition containing these compounds and their use in the treatment of complications of diabetes mellitus. The compounds of this series exhibit AGE breaking activity, which is essential for the treatment of diabetic and aging-related complications including **kidney disease,** nerve damage, atherosclerosis, retinopathy and dermatological conditions. The invention also extends to the method of reversing the discoloration of teeth resulting from nonenzymatic browning in the oral cavity which comprises administration of an amount effective to reverse pre-formed advanced glycosylation crosslinks. Maillard in 1912 found that reducing sugars, such as glucose and ribose react with proteins to form brown pigments. Further studies have shown that this is an irreversible non-enzymatic reaction, which occurs in several natural systems including stored foodstuff. Maillard reaction occurs in two stages, early and advanced. Initially, proteins react with glucose to form stable Amadori products, which subsequently cross-links to form advanced glycation end products (AGE). In most cases, the formation of AGE also accompanies browning of the proteins and increase in the fluorescence.

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

- **Novel nucleic acid and polypeptide**

  Inventor(s): Georgas, Kylie; (Brisbane, AU), Holmes, Gregory; (New York, NY), Kolle, Gabriel; (Brisbane, AU), Little, Melissa; (Brisbane, AU), Wilkinson, Lorine; (Brisbane, AU), Yamada, Carol Linda Susan; (Brisbane, AU), Yamada, Toshiya; (Brisbane, AU)

  Correspondence: Greenblum & Bernstein, P.L.C.; 1950 Roland Clarke Place; Reston; VA; 20191; US

  Patent Application Number: 20030082714

  Date filed: May 23, 2002

  Abstract: A novel isolated nucleic acid which corresponds to a gene located on human chromosome 2p21-16.3 is provided, and a polypeptide encoded thereby, together with mouse and chicken orthologs. The encoded polypeptides share a PGECCPLP motif and include an insulin-like growth factor binding domain, cysteine-rich repeats, an RGD motif and transmembrane domain, and interact with members of the transforming growth factor superfamily. The nucleic acids of the invention, and polypeptides encoded thereby, may be useful in the diagnosis and treatment of diseases including eye defects, neurodegenerative diseases, renal and **kidney disease,** bone and tooth abnormalities, wounds and skin damage.

  Excerpt(s): This application is a continuation of International Application No. PCT/AU00/01435, filed Nov. 24, 2000, which was published in English under PCT Article 21(2), the disclosure of which is incorporated by reference herein in its entirety, and which claims priority of Australian Application No. PQ4348, filed Nov. 26, 1999. THIS INVENTION relates to a novel isolated nucleic acid, and more particularly to an isolated nucleic which corresponds to a gene located on human chromosome 2p21-16.3. The invention also relates to an encoded polypeptide which interacts with members of the transforming growth factor beta (TGF.beta.) superfamily. The nucleic acids of the invention, and polypeptides encoded thereby, may be useful in the diagnosis and/or treatment of diseases including eye defects, neurodegenerative diseases, renal and **kidney disease,** bone and tooth abnormalities, wounds and skin damage without limitation thereto. Vertebrate development is a complex process involving a plethora of genes and gene products whose interactions direct crucial events such as cell fate, pattern formation, organogenesis and, at least to some extent, the development of intelligence and behaviour. Although an overview of this area is beyond the scope of this discussion, it has become clear that by understanding the genetic basis of development, the genetic basis of disease is also more properly understood.

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

- **Polycystic kidney disease PKD2 gene and uses thereof**

  Inventor(s): Mochizuki, Toshio; (Tokyo, JP), Somlo, Stefan; (Westport, CT)

  Correspondence: Amster, Rothstein & Ebenstein; Attorneys For Applicants; 90 Park Avenue; New York; NY; 10016; US

  Patent Application Number: 20020061520

  Date filed: January 2, 2001

  Abstract: The present invention provides a purified and isolated wild type PKD2 gene, as well as mutated forms of this gene. The present invention also provides one or more single-stranded nucleic acid probes which specifically hybridize to the wild type PKD2

gene or the mutated PKD2 gene, and mixtures thereof, which may be formulated in kits, and used in the diagnosis of ADPKD associated with the mutated PKD2 gene. The present invention also provides a method for diagnosing ADPKD caused by a mutated PKD2 gene, as well as a method for treating autosomal dominant polycystic **kidney disease** caused by a mutated PKD2 gene.

Excerpt(s): This invention is based upon the discovery by the inventors of the PKD2 gene associated with Autosomal Dominant Polycystic **Kidney Disease** ("ADPKD"), the "PKD2 gene" or "PKD2", and a novel protein encoded by this gene. The discovery of the PKD2 gene and the protein encoded by the gene will have important implications in the diagnosis and treatment of ADPKD caused by defects in the PKD2 gene. ADPKD is a genetically heterogeneous disorder that affects approximately 500,000 Americans and five million individuals world wide, and accounts for 8 to 10% of all end stage renal disease (ESRD) worldwide (Gabow, P. A. N. Eng. J. Med. 329:332 (1993)). Its principal clinical manifestation is bilateral renal cysts that result in chronic renal failure in about 45% of affected individuals by age 60 (Gabow, P. A., supra). Hypertension and liver cysts are common, and the involvement of other organ systems (Gabow, P. A., et al. Kidney Int. 38:1177 (1990); Chapman, A. B., et al. N. Eng. J. Med. 327:916 (1992); Hossack, K. F., et al. N. Enc. J. Med. 319:907 (1988); Torres, V. E., et al. Am. J. Kidney Dis. 22:513 (1993); Huston, J., et al. J. Am. Soc. Nephrol. 3:1871 (1993); Somlo, S., et al. J. Am. Soc. NeDhrol. 4:1371 (1993)) lends support to the view that polycystic **kidney disease** is a systemic disorder (Gabow, P. A., supra). To date, most forms of ADPKD have been associated with two genes, PKD1 and PKD2. The full genomic structure and cDNA sequence for the PKD1 gene has been identified (The International Polycystic **Kidney Disease** Consortium, Cell 81:289 (1995); The American PKD1 Consortium, Hum. Mol. Genet. 4:575 (1995)). Mutations in the PKD1 gene are suspected of causing 80-90% of all cases of ADPKD. The PKD2 gene has been localized on chromosome 4q21-23 and accounts for approximately 15% of affected families (Kimberling, W. J., et al. Genomics 18:467 (1993); Peters, D. J. M. and L. A. Sandkuijl Contrib. Neohrol. 97:128 (1992)). Prior to the present invention, however, the PKD2 gene had not been identified.

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

- **Potassium channel blocking agents**

  Inventor(s): Jensen, Bo Skaaning; (Copenhagen S, DK), Olesen, Soren Peter; (Klampenborg, DK), Peters, Dan; (Arlov, SE), Strobaek, Dorte; (Farum, DK), Teuber, Lene; (Vaerlose, DK)

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  Patent Application Number: 20020049246

  Date filed: December 29, 2000

  Abstract: This invention relates to novel potassium channel blocking agents, and their use in the preparation of pharmaceutical compositions.Moreover the invention is directed to pharmaceutical compositions useful for the treatment or alleviation of diseases or disorders associated with the activity of potassium channels, in particular asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic **kidney disease,** bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory diarrhoea, ischaemia, cerebral ischaemia, ischaemic hearth disease, angina pectoris, coronary hearth disease,

traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression.

Excerpt(s): This invention relates to novel potassium channel blocking agents, and their use in the preparation of pharmaceutical compositions. Moreover the invention is directed to pharmaceutical compositions useful for the treatment or alleviation of diseases or disorders associated with the activity of potassium channels, in particular asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic **kidney disease,** bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory diarrhoea, ischaemia, cerebral ischaemia, ischaemic hearth disease, angina pectoris, coronary hearth disease, traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labor, baldness, cancer, and immune suppression. Ion channels are transmembrane proteins, which catalyze the transport of inorganic ions across cell membranes. The ion channels participate in processes as diverse as the generation and timing of action potentials, synaptic transmissions, secretion of hormones, contraction of muscles, etc.

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

- **Substituted triazinyl acrylamide derivatives and methods of use**

  Inventor(s): Buchanan, John L.; (Brookline, MA), Kim, Joseph L.; (Wayland, MA), Novak, Perry M.; (Milford, MA), Nunes, Joseph J.; (Andover, MA), Patel, Vinod F.; (Acton, MA)

  Correspondence: U.S. Patent Operations/jwb; DEPT. 4300, M/s 27-4-a; Amgen INC.; One Amgen Center Drive; Thousand Oaks; CA; 91320-1799; US

  Patent Application Number: 20030139416

  Date filed: April 10, 2002

  Abstract: The invention encompasses compounds, analogs, prodrugs and pharmaceutically acceptable salts thereof, pharmaceutical compositions, uses and methods for prophylaxis and treatment of cancer and polycystic **kidney disease.**

  Excerpt(s): This application claims the benefit of U.S. Provisional Application No. 60/283,160, filed Apr. 11, 2001, which is hereby incorporated by reference. This invention is in the field of pharmaceutical agents and specifically relates to compounds, compositions, uses and methods for treating cancer and polycystic **kidney disease.** The invention relates to inhibitors of enzymes that catalyze phosphoryl transfer and/or that bind ATP/GTP nucleotides, compositions comprising the inhibitors, and methods of using and compositions comprising them are useful for treating or modulating disease in which phosphoryl transferases, including kinases, may be involved, symptoms of such disease, or the effect of other physiological events mediated by phosphoryl transferases, including kinases. The invention also provides for methods of making the

inhibitor compounds and methods for treating diseases in which one or more phosphoryl transferase, including kinase, activities is involved.

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

- **System for treating kidney disease in diabetic and non-diabetic patients**

  Inventor(s): Aoki, Thomas T.; (Sacramento, CA)

  Correspondence: Law Office OF Eric G. Masamori; 6520 Ridgewood Drive; Castro Valley; CA; 94552; US

  Patent Application Number: 20030176323

  Date filed: March 19, 2003

  Abstract: The present invention is a system capable of improving the entire metabolic process and through its multiplicity of effects on neurovascular reactivity, intraglomerular pressure and hemodynamics, arresting the progression of overt diabetic nephropathy, improving intraglomerular hemodynamics, and thus arresting the progression of diabetic nephropathy and therefore reducing the risk of development of End Stage Renal Disease. The current system is for the treatment of **kidney disease** using insulin pulses to a patient utilizing Chronic Intermittent Intravenous Insulin Therapy to achieve the slowing, stopping or reversing of **kidney disease** in both diabetic and non-diabetic patients.

  Excerpt(s): This application claims the benefit of U.S. patent application Ser. No. 09/881,826, filed on Jun. 15, 2001 which further claims the benefit of U.S. Provisional Patent Application No. 60/212,132 filed Jun. 16, 2000. This invention relates to the treatment of **kidney disease** in diabetic and non-diabetic patients. More specifically, the invention relates to a system for treating **kidney disease** in diabetic and non-diabetic patients with Chronic Intermittent Intravenous Insulin Therapy. Diabetic **kidney disease** (nephropathy) develops in 35 to 40% of patients with type 1 diabetes mellitus (DM) and in 10 to 60% of patients with type 2 DM depending upon the ethnic pool being studied. It is the most common cause of End-Stage Renal Disease (ESRD) in the United States. Experts generally have assumed that diabetic nephropathy is the result of hyperglycemia, whether alone or in combination with other factors, such as hypertension and genetic susceptibility to **kidney disease.** Two major recent clinical trials involving patients with type 1 DM (Diabetes Control and Complication Trial [DCCT]) and type 2 DM (United Kingdom Prospective Diabetes Study [UKPDS]) have demonstrated that improved glycemic control reduces the onset and the progression of early diabetic nephropathy to overt nephropathy in patients recently diagnosed with diabetes mellitus (DM) thereby giving additional credence to the hypothesis that a lack of glycemic control is the primary cause. Both of theses studies used recently diagnosed patients some of whom, although well controlled, went on to develop **kidney disease.** Since the DCCT and UKPDS studies demonstrated that near normalization of blood glucose level did not always result in a delay of the onset or progression of diabetic nephropathy, the hypothesis that euglycemia is the means for addressing this disease, is made suspect.

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

- **Therapeutic uses of milk mineral fortified food products**

  Inventor(s): Bastian, Eric Douglas; (Twin Falls, ID), Ward, Loren Spencer; (Twin Falls, ID)

  Correspondence: Banner & Witcoff; 1001 G Street N W; Suite 1100; Washington; DC; 20001; US

  Patent Application Number: 20030118662

  Date filed: December 5, 2001

  Abstract: Food products fortified with a therapeutically effective amount of milk mineral are administered for the treatment of high blood pressure, stroke, obesity, kidney stones, colon cancer, breast cancer, head and neck tumors, premenstrual syndrome, postpartum depression, hypertensive disorders of pregnancy, Type-2 diabetes, depression, asthma, inflammatory bowel disease, attention deficit disorder, migraine headaches, **kidney disease,** hypercholesterolaemia, congestive heart failure, or immune deficiency.

  Excerpt(s): The present invention is directed to milk mineral fortified food products and, more particularly to the treatment of high blood pressure, stroke, obesity, and various other disorders by administering food products fortified with a therapeutically effective amount of milk mineral. The natural milk minerals, especially calcium, magnesium, phosphorus, potassium and zinc, are of great importance in nutrition. Their importance is widely recognized for proper teeth and bone formation, as well as for skeletal structure development. During the period of late teenage to young adulthood, however, significant reductions in dietary calcium intake often occur. This is particularly true of the female population, where reduced dietary calcium intake usually occurs much earlier in life compared to their male counterparts. It has been observed that females are especially susceptible to a prolonged calcium deficit over their life span. This calcium deficit is believed to contribute to the greater incidence of osteoporosis in postmenopausal women. Calcium supplements and calcium-fortified foods containing calcium in such forms as calcium carbonate, calcium lactate, calcium citrate, calcium chloride, and calcium hydroxide have been proposed. These forms of calcium, however, can yield undesirable flavors and/or can strip desirable aroma and flavor compounds from food products. More significantly, these types of supplements deliver only calcium (no other minerals) and lack the balanced and pure form of the milk minerals (including calcium, phosphorus, potassium, magnesium, and zinc) present in milk and dairy products. As a result, these forms of calcium are less easily absorbed by the body and are inferior to milk and dairy products from a nutritional standpoint.

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

- **Treatment of diseases involving cyst formation**

  Inventor(s): Joly, Alison; (San Mateo, CA), Schreiner, George F.; (Los Altos Hills, CA), Stanton, Lawrence W.; (Redwood City, CA), White, R. Tyler; (Fremont, CA)

  Correspondence: Knobbe Martens Olson & Bear Llp; 2040 Main Street; Fourteenth Floor; Irvine; CA; 92614; US

  Patent Application Number: 20030008864

  Date filed: April 30, 2002

Abstract: The invention concerns the use of ligands of peripheral-type benzodiazepine receptors (PTBR) in the diagnosis and treatment of diseases involving cyst formation and in particular polycystic **kidney disease.** The invention further concerns the treatment of hypertension accompanying polycystic **kidney disease,** and pharmaceutical compositions and articles of manufacture for the treatment or diagnosis of the target disease or condition.

Excerpt(s): The present invention concerns the treatment of diseases involving cyst formation, such as polycystic **kidney disease.** The present invention also concerns various endogenous and exogenous ligands of peripheral-type benzodiazepine receptors, and in particular, their use in the prevention or treatment of cyst formation. There are several human diseases that result in the formation of cysts containing either semi-solid or fluid material. Benign cysts can occur, for example, in the ovary, spleen, lungs, kidney and liver, where they are often hereditary. Cysts can be acquired, as in diverticulosis of the intestines, or acquired as a secondary cause of an inherited disease, as in cystic fibrosis, or can be directly inherited, as in polycystic disease of the kidney, which can also affect the liver and brain. Renal cysts arise in the renal parenchyma, and begin as dilations or outpouchings from existing nephrons or collecting ducts or from the developmental counterparts of these structures. Renal cysts contain a fluid that presumably derives from their parent nephron and/or is a local secretion. They may be hereditary, developmental, or acquired, and may occur in the cortex, medulla or both, and may or may not be associated with other renal or systemic abnormalities. For further details see, for example, Brenner & Rector, The Kidney, Fourth Edition, 1991, Vol. I, pp. 1657-1659.

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

- **Triterpene saponins from soybeans for treating kidney disease**

  Inventor(s): Bureau, Dominique P.; (Guelph, CA), Collins, F. William; (Ottawa, CA), Holub, Bruce J.; (Guelph, CA), Philbrick, Diana J.; (Guelph, CA)

  Correspondence: Bereskin & Parr; Box 401; 40 King Street West; Toronto; ON; M5h 3y2; CA

  Patent Application Number: 20020107209

  Date filed: September 28, 2001

  Abstract: A method of treating polycystic **kidney disease** is described. The method involves administering soyasaponin B.sub.b to an animal in need thereof.

  Excerpt(s): This application claims the benefit under 35 USC.sctn.119(e) from U.S. Provisional patent application serial No. 60/236,341, filed Sep. 29, 2000. The present invention relates to methods and compositions for treating **kidney disease,** in particular polycystic **kidney disease.** Autosomal Polycystic **Kidney Disease** (ADPKD) is the most prevalent, potentially fatal, inherited disease affecting the human kidney with a reported incidence of 1 out of every 500 births. It has been estimated that 500,000 persons in North America suffer from this disease of which 30,000-75,000 are Canadians. Worldwide, almost 5 million persons suffer from this debilitating disease. Polycystic **kidney disease** results in enlarged, cyst-filled kidneys in the abdomen producing severe, unremitting back pain, early and progressive hypertension, frequent urinary tract infections and blood in the urine. PKD also has inflammatory and other clinical components. Approximately 45% of cases can be expected to progress to end-stage renal disease (fatal) before the age of 60, adding to health care costs for dialysis treatment,

hospitalization, premature morbidity due to cardiovascular and other disorders, surgeries, etc.

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

- **Use of alpha1beta1 integrin receptor inhibitors and TGF-beta1 inhibitors in the treatment of kidney disease**

  Inventor(s): Cosgrove, Dominic; (Omaha, NE)

  Correspondence: Mueting, Raasch & Gebhardt, P.A.; P.O. Box 581415; Minneapolis; MN; 55458; US

  Patent Application Number: 20020094956

  Date filed: March 12, 2002

  Abstract: The present invention provides methods for treating (i.e., delaying the onset of, slowing the progression of, and/or reversing) kidney disorders (e.g., renal glomerulonephritis and/or renal fibrosis). Certain of these methods involve administering an.alpha.1.beta.1 integrin receptor inhibitor optionally in combination with a TGF-.beta.1 inhibitor. The present invention also provides a mouse model for **kidney disease** wherein the mouse does not express a normal collagen type 4 composition in the GBM (i.e., it does not incorporate collagen.alpha.3(IV),.alpha.4(IV), and.alpha.5(IV) chains into its glomerular basement membrane) and does not express the.alpha.1.beta.1 integrin receptor.

  Excerpt(s): The present application is a Continuation-In-Part of U.S. patent application Ser. No. 09/150,485, filed on Sep. 9, 1998, which is a Continuation-In-Part of U.S. patent application Ser. No. 09/088,766, filed on Jun. 2, 1998, which claims the benefit of U.S. Provisional Application Serial No. 60/086,587, filed on May 22, 1998. This invention relates to the field of **kidney disease** (i.e., kidney disorder) characterized by glomerulonephritis and/or fibrosis. In particular, this invention relates to the use of a.alpha.1.beta.1 integrin receptor inhibitors in kidney disorders. Further, this invention relates to the use of.alpha.1.beta.1 integrin inhibitors in combination with TGF-.beta.1 inhibitors in kidney disorders. In the United States, approximately 12,000 people currently live with Alport syndrome. This inherited disorder results in progressive renal disease that is only treatable by dialysis and kidney transplant. Transplanted kidneys are usually rejected. Thus, alternative treatments are needed. However, there is currently no treatment that addresses the mechanism of the disease onset or progression. Thus, what is needed is a treatment method that attacks the mechanism of disease onset and/or progression, one that could substantially slow disease conditions, such as renal glomerulonephritis and renal fibrosis.

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

- **Use of anti-gp-39 antibodies for treatment and/or reversal of lupus and lupus associated kidney disease**

  Inventor(s): Burns, Christopher M.; (Lyme, NH), Noelle, Randolph J.; (Cornish, NH)

  Correspondence: Pillsbury Winthrop Llp; Intellectual Property Group; East Tower, Ninth Floor; 1100 New York Avenue, N.W.; Washington; DC; 20005-3918; US

  Patent Application Number: 20020058037

  Date filed: May 16, 2001

  Abstract: A method of treating lupus using anti-gp39 antibodies or fragments is provided. Such treatment has been shown to reverse disease, and in particular lupus-associated **kidney disease,** the major killer of lupus subjects.

  Excerpt(s): This application is a continuation of U.S. Ser. No. 09/054,488, filed Apr. 3, 1998, which is a continuation-in-part of U.S. Ser. No. 08/742,480, filed Nov. 1, 1996, which, in turn, is a continuation of Ser. No. 08/338,975, filed Nov. 14, 1994, abandoned, in turn, a continuation of Ser. No. 07/835,799, filed Feb. 14, 1992, now abandoned. The present invention relates to a counter-receptor, referred to alternatively in the literature as CD40CR, gp39, or most recently CD154 for the CD40 B-cell antigen, and to soluble ligands for this receptor, including fusion molecules comprising at least a portion of CD40 protein. It is based, at least in part, on the discovery that a soluble CD40/immunoglobulin fusion protein was able to inhibit helper T-cell mediated B-cell activation by binding to a novel 39 kD protein receptor on helper T-cell membranes. The present invention provides for a substantially purified CD40CR receptor; for soluble ligands of CD40CR, including anti-gp39 antibodies and fragments thereof, as well as fusion molecules comprising at least a portion of CD40 protein; and for methods of controlling B-cell activation which may be especially useful in the treatment of allergy or autoimmune disease. More specifically, the present invention relates to the use of anti-gp39 antibodies for treating systemic lupus erythematosus (SLE) or drug induced lupus. Studies by Mitchison, Benacerraf and Raff first suggested that physical interactions between T.sub.h and B-cells were essential in the development of humoral immune responses. Later studies documented that T.sub.h formed physical conjugates with class II major histocompatibility complex (MHC) compatible, antigen-presenting B-cells (Vitetta et al., Immunol. Rev., 99:193-239 (1987)) and that it was the B-cells within these conjugates that responded to T.sub.h (Barrett et al., J. Immunol., 143:1745-1754 (1989)). With the discovery that T.sub.h-derived lymphokines exerted potent growth and differentiative effects on B-cells, it was proposed that soluble factor(s) released in proximity by activated T.sub.h mediated the activation of the interacting B-cell. However, none of the molecularly cloned lymphokines, alone or in combination, manifested the ability to induce B-cell cycle entry. Unlike soluble factors, plasma membrane fractions from activated T.sub.h induced B-cell cycle entry (Hodgkin et al., J Immunol., 145:2025-2034 (1990); Noelle et al., J. Immunol., 146:1118-1124 (1991)). Studies using purified plasma membrane fractions from activated Th suggested that a protein expressed on the membrane of activated Th was responsible for initiating humoral immunity (Noelle et al., J. Immunol., 146:1118-1124 (1991); Bartlett et al., J. Immunol., 145:3956-3962 (1990)).

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

- **Xanthine oxidase inhibition as a strategy to alleviate oxidative impairment of vascular function**

  Inventor(s): Aslan, Mutay; (Antalya, TR), Freeman, Bruce A.; (Birmingham, AL), Ryan, Tom; (Birmingham, AL), Tarpey, Margaret; (Birmingham, AL), Townes, Tim; (Birmingham, AL)

  Correspondence: Bradley Arant Rose & White, Llp; Intellectual Property Department-nwj; 1819 Fifth Avenue North; Birmingham; AL; 35203-2104; US

  Patent Application Number: 20030158213

  Date filed: November 18, 2002

  Abstract: Disclosed is a method for alleviating the oxidative impairment of vascular function by inhibiting the activity of xanthine oxidase, or active forms thereof. Xanthine oxidase levels have been shown to be increased by a variety of conditions, including sickle cell disease. In the present disclosure, allopurinol is used to inhibit xanthine oxidase activity. As a result of the inhibition of xanthine oxidase,.NO levels in a subject can be maintained. In addition to sickle cell disease, allopurinol inhibition of xanthine oxidase may be used to treat other conditions, including, but not limited to, respiratory distress, **kidney disease,** liver disease, ischemia-reperfusion injury, organ transplant, sepsis, burns, viral infections and hemorrhagic shock.

  Excerpt(s): This disclosure claims the benefit of U.S. Provisional Patent Application No. 60/333,268, filed on Nov. 16, 2001. The present disclosure is directed to a method of using compounds which inhibit the activity of xanthine oxidase in order to alleviate the inhibition of vascular function caused by oxidative events and/or inflammatory conditions. The production of oxygen radical species, such as O.sub.2. and H.sub.2O.sub.2, have been know to cause tissue injury in living organisms and contribute to a wide variety of disease processes. Multiple features of sickle cell disease (SCD) reveal that inflammatory-derived oxidative reactions lead to impaired nitric oxide (.NO)-dependent vascular function. Nitric oxide is a free radical mediator of neurotransmitter, cell-mediated immunity and tissue redox reactions. In regulating endothelial-dependent vascular relaxation,.NO diffuses to target cells to stimulate cGMP production by guanylate cyclase and activate a chain of events in the vasculature including smooth muscle cell relaxation, inhibition of platelet aggregation and neutrophil margination and regulation of gene expression. In SCD, the production of.NO appears to be chronically activated to maintain vasodilation, as indicated by low baseline blood pressure, decreased pressor responses to angiotensin II, renal hyperfiltration and a tendency for priapism. Plasma arginine levels drop precipitously during pain crises, indicating a possible demand for, or insufficient synthesis of,.NO. The mechanisms underlying blood flow deprivation, the associated pain and consequent tissue injury in SCD remain poorly understood. If the tissue ischemia that is a hallmark of SCD resulted solely from polymerized, sickled red cells, occlusion of predominantly small blood vessels would occur. In contrast, stroke in SCD results from occlusion of large and medium-sized arteries (internal carotid and middle cerebral arteries). Importantly, levels of sickled erythrocytes or dense cells do not correlate with painful episodes and other manifestations of vascular occlusion, inferring that morbidity is due to vascular functional defects that occur in response to sickling, rather than mechanical effects of sickling. Increased oxidant production in the vasculature of SCD patients has been recognized for almost two decades. However, this disclosure reveals that the endogenous rate of production of superoxide (O.sub.2.--) and hydrogen peroxide (H.sub.2O.sub.2) by human sickle red cells is not significantly increased. In contrast, elevated plasma and vessel wall xanthine oxidase (XO) and myeloperoxidase

activity in SCD patients and SCD mice, and increased vessel wall O.sub.2.-- and H.sub.2O.sub.2 generation in SCD mice is observed. This is ascribed to the a) vessel wall binding of liver-derived circulating XO, released following repeated hepatic hypoxia-reoxygenation events, b) release and vessel wall binding of of neutrophil myeloperoxidase, and c) possible increased vessel wall expression of XO or other oxidases. This vascular inflammatory condition in SCD can induce O.sub.2.-- and H.sub.2O.sub.2 dependent inhibition of the salutary actions of.NO, while concomitantly yielding the potent and versatile reaction products, peroxynitrite (ONOO--) and nitrogen dioxide, oxidizing and nitrating species capable of further impairing vascular function. Thus, it is viewed that XO-derived reactive species impair nitric oxide-dependent systemic vascular function in SCD patients and contribute to the pathogenesis of acute sickle cell crises and end-organ damage. Therefore, a therapeutic regime to target and inhibit the XO-dependent production of O.sub.2. and H.sub.2O.sub.2 should be effective in treating SCD patients by preserving.NO functions and endothelial dependent function in SCD patients.

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 kidney disease, 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 "kidney disease" (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 kidney disease.

You can also use this procedure to view pending patent applications concerning kidney disease. Simply go back to **http://www.uspto.gov/patft/index.html**. Select "Quick Search" under "Published Applications." Then proceed with the steps listed above.

CHAPTER 7. BOOKS ON KIDNEY DISEASE

Overview

This chapter provides bibliographic book references relating to kidney disease. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, excellent sources for book titles on kidney disease 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 "kidney disease" (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 kidney disease:

- **Health Tips for Living with Polycystic Kidney Disease**

  Source: Kansas City, MO: PKD (Polycystic Kidney Disease) Foundation. 2001. 72 p.

  Contact: Available from PKD (Polycystic Kidney Disease) Foundation. 4901 Main Street, Suite 200, Kansas City, MO 64112-2634. (800) PKD-CURE. Fax: (816) 931-8655. Email: pkdcure@pkdcure.org Website: www.pkdcure.org. PRICE: $10.00 for PKD members; $15.00 for nonmembers. ISBN: 931365155.

  Summary: Polycystic kidney disease (PKD) has two hereditary forms: autosomal dominant (ADPKD), the most common of all life-threatening genetic diseases, or autosomal recessive (ARPKD), a relatively rare disease that often causes significant mortality in the first month of life. Cysts are sacs of fluid that cause the kidney to enlarge and that can hinder the kidney's filtering ability. Recent research has found certain dietary modifications, hypertension (high blood pressure) treatments, and

lifestyle changes to have a favorable, progression-slowing impact on PKD. This book offers strategies for healthy living for people with ADPKD. The book is divided into four sections: a comprehensive section regarding diet and ADPKD; a section reviewing issues of pregnancy and estrogen use for women with PKD; a section dealing with chronic pain and exercise; and a section on where to go in the renal community for support and information. The book concludes with a list of websites for additional information, a listing of National ESRD (End Stage Renal Disease) Network Organizations, and appendices that list sodium content of common foods, high quality protein vegetarian combinations, and special menus. 4 figures.

- **Proceedings of the Fifth International Workshop on Polycystic Kidney Disease**

  Source: Kansas City, MO: PKR Foundation. 1993. 181 p.

  Contact: Available from PKR Foundation. 4901 Main Street, Suite 320, Kansas City, MO 64112. (800) 753-2873. PRICE: $33.95 for members; $39 for nonmembers. ISBN: 096145671X.

  Summary: The articles gathered in this book are the result of presentations of papers on research at the 5th International Workshop on Polycystic Kidney Disease, held in Kansas City, Missouri in June 1992. Twenty-two brief chapters are presented in four sections: the genetics of polycystic kidney disease (PKD); the clinical aspects of autosomal dominant PKD; acquired renal cystic disease; and the cell biology of PKD. These chapters include brief reference lists. The remainder of the book consists of 41 abstracts accepted for poster presentation at the conference.

- **PKD Patient's Manual: Understanding and Living with Autosomal Dominant Polycystic Kidney Disease. 2nd ed**

  Source: Kansas City, MO: Polycystic Kidney Research Foundation (PKR Foundation). 1995. 66 p.

  Contact: Available from Polycystic Kidney Research Foundation (PKR Foundation). 4901 Main Street, Suite 320, Kansas City, MO 64112-2674. (800) 753-2873 or (816) 931-2600. PRICE: $10.00 (members); $15.00 (nonmembers), as of 1996. ISBN: 0961456744.

  Summary: This book provides information about autosomal dominant polycystic kidney disease (ADPKD) to those who have the disease, those who are at risk due to an affected parent, and interested family members and friends. Topics include the nature of the disease and its prevalence, how ADPKD is inherited, diagnostic tests, basic kidney anatomy and physiology, kidney cysts and how they form, signs and symptoms of ADPKD, the role of dialysis or transplantation in the treatment, pregnancy in women with ADPKD, preventive diet therapy, managing children with ADPKD, symptoms of kidney failure, and the role of self care. The book is written primarily in question and answer format, with most medical terms avoided or explained in layperson's language. 12 figures. 1 table. 5 references.

- **Primer on Kidney Diseases. 2nd ed**

  Source: San Diego, CA: Academic Press. 1998. 542 p.

  Contact: Available from Academic Press. Order Fulfillment Department, 6277 Sea Harbor Drive, Orlando, FL 32887. (800) 321-5068 or (407) 345-3800. Fax (800) 874-6418 or (407) 345-4060. E-mail: apbcs@harcourtbrace.com. Website: www.apnet.com. PRICE: $57.95 plus shipping and handling. ISBN: 0122990900.

Summary: This comprehensive textbook on kidney diseases is designed for medical students, house staff, and practitioners. The text offers a summary of the management of renal disease and fluid and electrolyte disorders. The 79 chapters are categorized in 11 sections, covering renal function and its assessment, electrolyte disorders, glomerular disease, the kidney in systemic disease, acute renal failure, drugs and the kidney, hereditary renal diseases, tubulointerstitial diseases, the kidney in special circumstances, chronic renal disease, and hypertension. Specific chapter topics include the characteristics of kidney function in the very young and in the very old, tubulointerstitial diseases, analgesic abuse nephropathy and the effects of NSAIDs on the kidneys, hematuria (blood in the urine), proteinuria, renal imaging techniques, metabolic acidosis and alkalosis, edema and the clinical use of diuretics, immunopathogenesis, minimal change nephropathy, IgA nephropathy, Goodpasture's syndrome, renal function in congestive heart failure, renal function in liver disease, renal manifestations of systemic lupus erythematosus, diabetic nephropathy, dysproteinemias and amyloidosis, renal and urologic complications of cancer and its treatment, hemolytic uremic syndrome, the renal manifestations of HIV, interstitial nephritis, sickle cell nephropathy, Alport's syndrome, medullary cystic disease, tubulointerstitial disease, lead nephrotoxicity, lithium induced renal disease, medullary sponge kidney, obstructive uropathy, nephrolithiasis (kidney stones), urinary tract infections, the kidney in pregnancy, the uremic syndrome, hemodialysis and hemofiltration, peritoneal dialysis, nutrition and renal disease, renal osteodystrophy, renal transplantation, and the pathogenesis of hypertension. Each chapter is written by an established expert in the field. The book is illustrated with full color and black and white photographs, figures, and tables. Each chapter concludes with suggested readings. An extensive subject index concludes the text.

- **Tasty, Tender Temptations: Recipes for Soft, High-Fiber, Low-Salt Meals for Folks with Kidney Disease**

  Source: Roanoke, TX: Niche Pharmaceuticals, Inc. 1997. 19 p.

  Contact: Available from Niche Pharmaceuticals, Inc. 200 North Oak Street, Roanoke, TX 76262. (800) 677-0355. Fax (817) 491-3533. PRICE: Single copy free to health professionals; bulk copies available.

  Summary: This cookbook features recipes that are acceptable for a person following a renal diet and that combine high fiber and low salt foods in an easy to ingest and easy to digest form. The recipes are designed to help kidney disease patients who have trouble chewing or swallowing and who may be at increased risk of malnutrition as they try to follow the recommended renal diet. The introductory material discusses the importance of dietary fiber (including the use of supplements), the role of caloric intake, and the individual recommendations for protein foods, starches, vegetables, and fruits. The recipes begin with three basic sauces: a white sauce, a brown sauce, and a tomato sauce; the nutritional values (calories, protein, sodium, potassium, and phosphorus) are provided for each. The cookbook then provides recipes for lasagna, chicken pot pie, beef burgundy, beef stroganoff, shrimp creole, mock stuffed crab, Garden-roni, curried egg, and Dialyzing potatoes. All of the recipes include the supplemental fiber product, Unifiber, manufactured by the company that created the cookbook. All of the recipes include a nutrient analysis that notes calories, protein, sodium, potassium, and phosphorus amounts. The cookbook is spiral bound for ease of use.

- **Kidney Disease and Your Diet**

  Source: Hamilton, Ontario: St. Joseph's Hospital, Nephrology Program. 1996. 40 p.

Contact: Available from Veena Juneja, Renal Dietitian. St. Joseph's Hospital, 50 Charlton Avenue East, Hamilton, Ontario, L8N 4A6, Canada. PRICE: $10.00 per copy plus $3.00 shipping and handling; for 10 or more copies, $5.00 per copy plus shipping and handling.

Summary: This patient education booklet gives readers information about the interplay of diet and kidney disease. After an introduction reviewing general principles about the impact of diet on kidney disease, the author discusses protein, potassium, phosphorus, sodium, herbs and spices, maintaining a healthy weight, fluids, reading labels, and eating at restaurants. Written in nontechnical language, the booklet focuses on helping readers find practical strategies for implementing the recommended nutritional guidelines. A sample menu plan is included for readers to complete with the help of their health care provider. Also included are brief lists of foods to include and avoid in each of the nutritional categories. A list of recommended cookbooks concludes the booklet. 4 figure. 10 tables.

- **Kidney Disease in Primary Care**

  Source: Baltimore, MD: Williams and Wilkins. 1998. 297 p.

  Contact: Available from Williams and Wilkins. 351 West Camden Street, Baltimore, MD 21201-2436. (800) 638-0672 or (410) 528-4223. Fax (800) 447-8438 or (410) 528-8550. E-mail: custserv@wwilkins.com. PRICE: $39.95. ISBN: 0683300571.

  Summary: This textbook provides primary care physicians with practical approaches to common clinical problems of kidney diseases. Interpretation of common radiographic and laboratory techniques are discussed, as are approaches to fluid and electrolyte disturbances. The first seven chapters cover urinalysis and assessment of urinary electrolytes; radiologic studies of common renal diseases; nuclear imaging of the genitourinary system; evaluating renal function in acute and chronic renal failure; hyponatremia and hypernatremia (sodium); hypokalemia and hyperkalemia (potassium); and hypomagnesemia and hypermagnesemia (magnesium). The problem of patients presenting with elevated levels of urea and creatinine is discussed in depth, as are outpatient issues such as the proper approach to proteinuria and management strategies for hypertension, heart failure, edema, diabetes, glomerulonephritis, polycystic kidney disease, kidney stones, and urinary tract infections. In addition, the authors cover issues of patient counseling, proper drug dosing, and nutritional approaches. Kidney transplantation is not covered in depth; however, one chapter addresses the management of renal transplant patients. Each of the 24 chapters is written by nephrology experts and include an outline of content, specific diagnostic and management strategies, suggestions for when to refer a patient, and suggested readings. A subject index concludes the textbook.

- **Primer on Kidney Diseases. 3rd ed**

  Source: Orlando, FL: Academic Press. 2001. 511 p.

  Contact: Available from Academic Press. Order Fulfillment Department, 6277 6418. E-mail: apbcs@harcourtbrace.com. Website: www.apnet.com. PRICE: $59.95; plus shipping and handling. ISBN: 122991001.

  Summary: This third edition of the National Kidney Foundation's popular Primer on Kidney Diseases provides a current review of the pathophysiology, diagnosis, and management of kidney disease, fluid and electrolyte disorders, hypertension, dialysis, and renal transplantation. The text includes 72 chapters in eleven sections: the structure

and function of the kidney and their clinical assessment; acid-base, fluid, and electrolyte disorders; glomerular diseases; the kidney in systemic disease; acute renal failure; drugs and the kidney; hereditary renal disorders; tubulointerstitial nephropathies and disorders of the urinary tract; the kidney in special circumstances, including pregnancy and aging; chronic renal failure and its therapy; and hypertension. Each chapter is written by an established expert in the field and concludes with a bibliography. The text is illustrated with black-and-white and full-color photographs, charts, and figures. 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 "kidney disease" at online booksellers' Web sites, you may discover non-medical books that use the generic term "kidney disease" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "kidney disease" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **A short textbook of kidney disease** by Adrian Peter Douglas; ISBN: 0272755141; http://www.amazon.com/exec/obidos/ASIN/0272755141/icongroupinterna
- **Amyloidosis and kidney disease (SuDoc HE 20.3302:AM 9)** by U.S. Dept of Health and Human Services; ISBN: B000114UKO; http://www.amazon.com/exec/obidos/ASIN/B000114UKO/icongroupinterna
- **Analgesic and Nsaid-Induced Kidney Disease (Oxford Monographs on Clinical Nephrology)** by J.H. Stewart (Editor), Columba Stewart (1995); ISBN: 019261956X; http://www.amazon.com/exec/obidos/ASIN/019261956X/icongroupinterna
- **Autosomal Dominant Polycystic Kidney Desease: Seminar on Autosomal Dominant Polycystic Kidney Disease, Vimercate, June 18, 1994 (Contributions to Nephrology, Vol 115)** by P. Seminar on Autosomal Dominant Polycystic Kidney Disease / Serbelloni (Editor), A. Sessa (1995); ISBN: 3805560907; http://www.amazon.com/exec/obidos/ASIN/3805560907/icongroupinterna
- **Coping with Kidney Disease : A 12-Step Treatment Program to Help You Avoid Dialysis** by Mackenzie Walser (Author), Betsy Thorpe (Author) (2004); ISBN: 0471274232; http://www.amazon.com/exec/obidos/ASIN/0471274232/icongroupinterna
- **Draft program initiative concepts for FY 2000 program plan submitted to the National Diabetes and Digestive and Kidney Diseases Advisory Council (SuDoc HE 20.3302:IN 8/2/DRAFT)** by U.S. Dept of Health and Human Services; ISBN: B000111JCG; http://www.amazon.com/exec/obidos/ASIN/B000111JCG/icongroupinterna
- **Eating Well, Living Well With Kidney Disease** by Steven Schwab, et al; ISBN: 0670866334; http://www.amazon.com/exec/obidos/ASIN/0670866334/icongroupinterna

- **Handbook of Drug Therapy in Liver and Kidney Disease** by Robert W. Schrier; ISBN: 0316774855; http://www.amazon.com/exec/obidos/ASIN/0316774855/icongroupinterna
- **Hereditary Kidney Diseases (Contributions to Nephrology, V. 122.)** by A. Sessa (Editor) (1997); ISBN: 3805565518; http://www.amazon.com/exec/obidos/ASIN/3805565518/icongroupinterna
- **High blood pressure and kidney disease (SuDoc HE 20.3323/3:B 62)** by U.S. Dept of Health and Human Services; ISBN: B0001158G4; http://www.amazon.com/exec/obidos/ASIN/B0001158G4/icongroupinterna
- **Hypertension in Kidney Disease (Developments in Nephrology, 14)** by Jhoong, S. Cheigh, et al (1986); ISBN: 0898387973; http://www.amazon.com/exec/obidos/ASIN/0898387973/icongroupinterna
- **Kidney Disease** by Rondo Cameron, et al; ISBN: 0192613294; http://www.amazon.com/exec/obidos/ASIN/0192613294/icongroupinterna
- **Kidney disease : present status**; ISBN: 0683016717; http://www.amazon.com/exec/obidos/ASIN/0683016717/icongroupinterna
- **Kidney Disease in Primary Care** by Anil K. Mandal (Editor), N. Stanley Nahman (Editor); ISBN: 0683300571; http://www.amazon.com/exec/obidos/ASIN/0683300571/icongroupinterna
- **Kidney disease in the young** by Elvira Goettsch; ISBN: 0721641407; http://www.amazon.com/exec/obidos/ASIN/0721641407/icongroupinterna
- **Kidney Disease: Hematologic and Vascular Problems (Perspectives in Nephrology and Hypertension)** by Rawle M. McIntosh (Editor), et al; ISBN: 0471019216; http://www.amazon.com/exec/obidos/ASIN/0471019216/icongroupinterna
- **Kidney Disease: The Facts (Oxford Medical Publications)** by Stewart Cameron, J. Stewart Cameron; ISBN: 0192615947; http://www.amazon.com/exec/obidos/ASIN/0192615947/icongroupinterna
- **Kidney physiology and kidney disease : an introduction to nephrology** by David L. Maude; ISBN: 0397520794; http://www.amazon.com/exec/obidos/ASIN/0397520794/icongroupinterna
- **Kidney Transplant Rejection: Diagnosis and Treatment (Kidney Disease, Vol. 9)** by James F. Burdick, et al; ISBN: 0824784871; http://www.amazon.com/exec/obidos/ASIN/0824784871/icongroupinterna
- **Laboratory Diagnosis of Kidney Diseases** by F. William Sunderman (1970); ISBN: 0875270778; http://www.amazon.com/exec/obidos/ASIN/0875270778/icongroupinterna
- **Meal Planning for People With Kidney Disease** by Sachiko St Jeor; ISBN: 0874801184; http://www.amazon.com/exec/obidos/ASIN/0874801184/icongroupinterna
- **New Perspectives in Diagnosis and Treatment of Kidney Disease (Contributions to Nephrology, Vol 55)** by G. D'Amico, G. Colasanti (Editor) (1987); ISBN: 380554393X; http://www.amazon.com/exec/obidos/ASIN/380554393X/icongroupinterna
- **Pediatric Kidney Disease** by Chester M. Edelmann (1992); ISBN: 0316211087; http://www.amazon.com/exec/obidos/ASIN/0316211087/icongroupinterna

- **Polycystic Kidney Disease** by Michael L. Watson (Editor), et al (1996); ISBN: 0192625780;
http://www.amazon.com/exec/obidos/ASIN/0192625780/icongroupinterna
- **Polycystic Kidney Disease (Contributions to Nephrology, Vol 97)** by M.H. Breuning, et al (1992); ISBN: 3805555865;
http://www.amazon.com/exec/obidos/ASIN/3805555865/icongroupinterna
- **Potassium in Cardiovascular and Renal Medicine: Arrhythmias, Myocardial Infarction, and Hypertension (Kidney Disease Series, Vol 6)** by Paul K. Whelton, Andrew Whelton; ISBN: 0824773764;
http://www.amazon.com/exec/obidos/ASIN/0824773764/icongroupinterna
- **Prevention of Kidney Disease and Long-Term Survival** by M. M. Avram; ISBN: 0306409658;
http://www.amazon.com/exec/obidos/ASIN/0306409658/icongroupinterna
- **Primer on Kidney Diseases** by Arthur Greenberg (Author), et al; ISBN: 0122991001;
http://www.amazon.com/exec/obidos/ASIN/0122991001/icongroupinterna
- **Problems in diagnosis and management of polycystic kidney disease : proceedings of the First International Workshop on Polycystic Kidney Disease**; ISBN: 0961456701;
http://www.amazon.com/exec/obidos/ASIN/0961456701/icongroupinterna
- **Progress in Clinical Kidney Disease and Hypertension** (1985); ISBN: 3136619013;
http://www.amazon.com/exec/obidos/ASIN/3136619013/icongroupinterna
- **Rare Kidney Diseases (Contributions to Nephrology, Vol 136)** by Arrigo Schieppati (Editor), et al (2001); ISBN: 3805572786;
http://www.amazon.com/exec/obidos/ASIN/3805572786/icongroupinterna
- **Renal Tubular Disorders: Pathophysiology, Diagnosis, and Management (Kidney Disease)** by Harvey C. Gonick (Editor); ISBN: 0824773713;
http://www.amazon.com/exec/obidos/ASIN/0824773713/icongroupinterna
- **Seminar on Immunological Aspects of Kidney Diseases in Children** by George D. Maragos (Editor) (1981); ISBN: 3805534884;
http://www.amazon.com/exec/obidos/ASIN/3805534884/icongroupinterna
- **Social Work and Dialysis: The Medical and Psychosocial Aspects of Kidney Disease** by Carrie L. Fortner-Frazier; ISBN: 0520036743;
http://www.amazon.com/exec/obidos/ASIN/0520036743/icongroupinterna
- **The kidney diseases dictionary (SuDoc HE 20.3302:K 54/4)** by U.S. Dept of Health and Human Services; ISBN: B0001128U8;
http://www.amazon.com/exec/obidos/ASIN/B0001128U8/icongroupinterna
- **The Official Patient's Sourcebook on Polycystic Kidney Disease** by James N., M.D. Parker (Editor), et al (2002); ISBN: 0597832277;
http://www.amazon.com/exec/obidos/ASIN/0597832277/icongroupinterna
- **The Struggle for Life : A Psychological Perspective of Kidney Disease and Transplantation** by Lyndsay S. Baines (Author), Rahul M. Jindal (Author) (2003); ISBN: 0865693234;
http://www.amazon.com/exec/obidos/ASIN/0865693234/icongroupinterna

The National Library of Medicine Book Index

The National Library of Medicine at the National Institutes of Health has a massive database of books published on healthcare and biomedicine. Go to the following Internet site, **http://locatorplus.gov/**, and then select "Search LOCATORplus." Once you are in the search area, simply type "kidney disease" (or synonyms) into the search box, and select "books only." From there, results can be sorted by publication date, author, or relevance. The following was recently catalogued by the National Library of Medicine:[11]

- **A short textbook of kidney disease [by] Adrian P. Douglas and David N. S. Kerr.** Author: Douglas, Adrian P.; Year: 1968; Philadelphia, Lippincott [1968]
- **A study of hemolytic anemia and kidney disease in conventional and germ-free New Zealand black mice.** Author: Unni, K. Krishnan,; Year: 1970; [Minneapolis] 1970
- **Benefit-cost analysis of kidney disease programs, by David A. LeSourd, Mark E. Fogel [and] Donald R. Johnston.** Author: LeSourd, David A.; Year: 1969; Washington, for sale by the Supt. of Docs., U. S. Govt. Print. Off. [1969]
- **Comprehensive health planning and regional medical programs: hearings before the Subcommittee on Public Health and Welfare of the Committee on Interstate and Foreign Commerce, House of Representatives, Ninety-first Congress, second session on H.R. 15960 a bill entitled "Health Services Improvement Act of 1970" (and similar bills) and H.R. 17570 a bill entitled "Heart Disease, Cancer, Stroke, and Kidney Disease Amendments of 1970" (and similar bills) June 1, 2, 3, and 4, 1970.** Author: United States. Congress. House. Committee on Interstate and Foreign Commerce. Subcommittee on Public Health and Welfare.; Year: 1983; Washington: U.S. G.P.O., 1970
- **Functional diagnosis of kidney disease, with especial reference to renal surgery; clinical experimental investigations by Leopold Casper and Paul Friederich Richter. Tr. by Robert C. Bryan and Henry L. Sanford.** Author: Casper, Leopold,; Year: 1974; Philadelphia, Blakiston, 1903
- **Heart Disease, Cancer, Stroke, and Kidney Disease Amendments of 1970: hearings before the Subcommittee on Health of the Committee on Labor and Public Welfare, United States Senate, Ninety-first Congress, second session, on S. 3355. S. 3443. and related bills, February 17 and 18, 1970.** Author: United States. Congress. Senate. Committee on Labor and Public Welfare. Subcommittee on Health.; Year: 1982; Washington: U.S. G.P.O., [1970?]-
- **Hereditary, developmental, and immunologic aspects of kidney disease, edited by Jack Metcoff.** Author: Metcoff, Jack,; Year: 1967; [Evanston, Ill.] Published for the National
- **Hospital categorization guidelines; optimal criteria for hospital resources for the care of patients with heart disease, cancer, stroke, and end-stage kidney disease.** Author: Joint Commission on Accreditation of Hospitals.; Year: 1977; [Chicago, c1974]

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[11] In addition to LOCATORPlus, in collaboration with authors and publishers, the National Center for Biotechnology Information (NCBI) is currently adapting biomedical books for the Web. The books may be accessed in two ways: (1) by searching directly using any search term or phrase (in the same way as the bibliographic database PubMed), or (2) by following the links to PubMed abstracts. Each PubMed abstract has a "Books" button that displays a facsimile of the abstract in which some phrases are hypertext links. These phrases are also found in the books available at NCBI. Click on hyperlinked results in the list of books in which the phrase is found. Currently, the majority of the links are between the books and PubMed. In the future, more links will be created between the books and other types of information, such as gene and protein sequences and macromolecular structures. See **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books**.

- **Kidney disease: case studies: a compilation of 61 clinical studies** Author: Parrish, Alvin E.,; Year: 1970; Garden City, N. Y.: Medical Examination Pub. Co., c1980; ISBN: 087488022X
  http://www.amazon.com/exec/obidos/ASIN/087488022X/icongroupinterna
- **Kidney disease and artificial kidneys.** Author: National Institute of Arthritis and Metabolic Diseases (U.S.); Year: 1926; Bethesda, Md., For sale by the Supt. of Docs., U. S. Govt. Print Off., Washington, 1971
- **Kidney disease from the physician's viewpoint, by Rolfe Floyd.** Author: Floyd, Rolfe,; Year: 1934; New York city, J. T. Dougherty [c1926]
- **Kidney disease, the facts** Author: Cameron, Stewart.; Year: 1981; Oxford; New York: Oxford University Press, 1981; ISBN: 0192612394
- **Kidney disease: program analysis; a report to the Surgeon General, prepared under direction of Office of Program Planning and Evaluation, Office of the Surgeon General [Benjamin T. Burton, chairman.** Author: United States. Public Health Service. Kidney Disease Program Analysis Group.; Year: 1963; Washington, U. S. Public Health Service, 1967]
- **Kidney disease; case studies. A compilation of 56 case histories representing nephrologic problems.** Author: Parrish, Alvin E.,; Year: 1975; Flushing, N. Y., Medical Examination Pub. Co. [c1975]; ISBN: 087488022X
  http://www.amazon.com/exec/obidos/ASIN/087488022X/icongroupinterna
- **Kidney disease; prevention and control; guidelines for community programs of chronic disease control, May 1969.** Author: Kidney Disease Control Program (Division of Chronic Disease Programs); Year: 1969; Washington, For sale by the Supt. of Docs., U. S. Govt. Print. Off. [1969]
- **Non-invasive diagnosis of kidney disease** Author: Lubec, Gert.; Year: 1961; Basel; New York: Karger, 1983; ISBN: 380553051X
  http://www.amazon.com/exec/obidos/ASIN/380553051X/icongroupinterna
- **Polycystic kidney disease in children.** Author: Uhler, Walter Miller,; Year: 1937; [Minneapolis] 1951
- **Practical talks on kidney disease, by Edward Weiss.** Author: Weiss, Edward,; Year: 1903; Springfield, Ill., Baltimore, Md., C. C. Thomas [c1937]
- **The clinical management of horseshoe kidney; a study of horseshoe kidney disease, its etiology, pathology, symptomatology, diagnosis and treatment, by Robert Gutierrez. with a foreword by Dr. Edmond Papin. 52 illustrations.** Author: Gutierrez, Robert,; Year: 1975; New York, P. B. Hoeber, inc., 1934
- **The economic cost of kidney disease and related diseases of the urinary system, by Jerome B. Hallan, Benjamin S. H. Harris III [and] Albert V. Alhadeff.** Author: Hallan, Jerome B.; Year: 1970; Washington, For sale by the Supt. of Docs., U. S. Govt. Print. Off. [1970]

Chapters on Kidney Disease

In order to find chapters that specifically relate to kidney disease, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and kidney disease 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 "kidney disease" (or synonyms) into the "For these words:" box. The following is a typical result when searching for book chapters on kidney disease:

- **Chronic Kidney Disease**

  Source: In U.S. Department of Health and Human Services and National Institutes of Health. Healthy People 2010. Conference Edition. Washington, DC: U.S. Government Printing Office. 2000. p. 4-1-4-28.

  Contact: Available from U.S. Government Printing Office. Superintendent of Documents, Mail Stop: SSOP, Washington, DC 20402-9328. (202) 783-3238. Website: www.health.gov/healthypeople. PRICE: Full-text available online at no charge.

  Summary: The United States government program called Healthy People 2010 is designed to achieve two overarching goals: increase quality and years of healthy life and eliminate health disparities. These two goals are supported by specific objectives in 28 focus areas. The Healthy People 2010 project outlines a comprehensive, nationwide health promotion and disease prevention agenda. This chapter on chronic kidney disease is from a two-volume set of publications that describe the Healthy People 2010 project. The goal in this area is to reduce new cases of chronic kidney disease and its complications, disability, death, and economic costs. The chapter also includes an overview that discusses issues and trends, disparities, and opportunities; a description of interim progress toward Year 2000 Objectives; a summary of the objectives for Health People 2010; a detailed discussion of the Healthy People 2010 objectives in this area; a listing of related objectives from other focus areas; a glossary of terms; and a list of references. Each section includes data provided in chart format. 1 figure. 12 tables. 61 references.

- **Kidney Diseases in Diabetes**

  Source: in Harris, M.I., et al., eds., for the National Diabetes Data Group (NDDG). Diabetes in America. 2nd ed. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health. 1995. p. 349-400.

  Contact: Available from National Diabetes Information Clearinghouse (NDIC). 1 Information Way, Bethesda, MD 20892-3560. (800) 860-8747 or (301) 654-3327. Fax (301) 634-0716. E-mail: ndic@info.niddk.nih.gov. Also available at http://www.niddk.nih.gov/. PRICE: Full-text book and chapter available online at no charge; book may be purchased for $20.00. Order number: DM-96 (book).

  Summary: This chapter on kidney diseases in diabetes is from a compilation and assessment of data on diabetes and its complications in the United States. After a brief discussion of epidemiology and costs, the authors cover terminology; the pathophysiology of diabetic renal disease; diabetic glomerulosclerosis; protein excretion; glomerular hemodynamic function; renal morphology; selective glomerular permeability; the incidence and prevalence of elevated urinary albumin excretion; elevated urinary albumin excretion as a risk factor for death; end-stage renal disease (ESRD); the risk factors for diabetic renal disease, including familial and genetic factors, hypertension, hyperglycemia, plasma prorenin activity, lipids, autonomic neuropathy, pregnancy, diet, smoking, and drug nephrotoxicity; renal disease and its relationship to other complications; the treatment options for diabetic renal disease, including metabolic control, blood pressure control and ACE inhibitors, and dietary modification; survival of ESRD patients; and the economic impact of renal replacement therapy. A final section discusses other kidney diseases associated with diabetes, including

infection, renal papillary necrosis, and radiocontrast-induced kidney failure. 20 appendices. 35 figures. 20 tables. 306 references.

- **Multicystic Dysplastic Kidney Disease**

  Source: in Gearhart, J.P.; Rink, R.C.; Mouriquand, P.D. Pediatric Urology. Philadelphia, PA: W.B. Saunders Company. 2001. p. 279-287.

  Contact: Available from Elsevier, Health Sciences Division. The Curtis Center, 625 Walnut Street, Philadelphia, PA 19106. (800) 523-1649. E-mail: custserv.ehs@elsevier.com. Website: www.us.elsevierhealth.com. PRICE: $239.00 plus shipping and handling. ISBN: 072168680X.

  Summary: This chapter on multicystic dysplastic kidney disease is from a comprehensive textbook on pediatric urology that emphasizes the pathophysiology of various disorders. The authors note that dysplasia is identified on microscopic examination by the presence of primitive ducts and metaplastic cartilage. It can occur in varied amounts from isolated areas to encompassing the entire kidney. Dysplasia accompanied by cysts is referred to as multicystic dysplasia, whereas dysplasia with a preponderance of cysts encompassing the kidney is known as multicystic dysplastic kidney disease (MCDK). Three morphological types of MCDK exist. Once antenatal screening ultrasonography became routine, a greater number of MCDKs were suspected, and the management as well as the potential complications needed to be elucidated. The authors review histology, etiology, clinical features, diagnosis, natural history, and treatment. 6 figures. 116 references.

Directories

In addition to the references and resources discussed earlier in this chapter, a number of directories relating to kidney disease have been published that consolidate information across various sources. The Combined Health Information Database lists the following, which you may wish to consult in your local medical library:[12]

- **Digestive Diseases Centers Program of the National Institute of Diabetes and Digestive and Kidney Diseases**

  Source: Bethesda, MD: National Institutes of Health. National Institute of Diabetes and Digestive and Kidney Diseases. 1991. 26 p.

  Contact: Available from Office of Health Research Reports. National Institutes of Health, NIDDK, 9000 Rockville Pike, Building 31, Room 9A04, Bethesda, MD 20892. (301) 496-3583. PRICE: Single copy free.

  Summary: This document describes 12 digestive diseases centers, each funded by the National Institute of Diabetes and Digestive and Kidney Diseases grant program. A center grant is generally a large, multidisciplinary allocation intended to stimulate research in digestive diseases by pooling resources and attracting young investigators as well as seasoned researchers from other fields. This directory presents information

[12] You will need to limit your search to "Directory" and "kidney disease" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find directories, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Select your preferred language and the format option "Directory." Type "kidney disease" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months.

about the programs, investigators, administrative structures, histories, research, and recent scientific advances for each of the 12 digestive diseases centers. Facilities included are: the Massachusetts General Hospital Center for the Study of Inflammatory Bowel Disease; the University of Chicago Digestive Diseases Research Center; the University of North Carolina Center for Gastrointestinal Biology and Disease; the Stanford University School of Medicine Digestive Disease Center; the Center for Ulcer Research and Education at the University of California, Los Angeles; the Yale Liver Research Center; the Liver Center at the University of California, San Francisco; the University of Colorado Hepatobiliary Research Center; the Albert Einstein Liver Research Center; the Harvard Digestive Diseases Center; the University of Michigan Gastrointestinal Peptide Research Center; and the Center for Gastrointestinal Research on Absorptive and Secretory Processes, Tufts University. (AA-M).

CHAPTER 8. MULTIMEDIA ON KIDNEY DISEASE

Overview

In this chapter, we show you how to keep current on multimedia sources of information on kidney disease. We start with sources that have been summarized by federal agencies, and then show you how to find bibliographic information catalogued by the National Library of Medicine.

Video Recordings

An excellent source of multimedia information on kidney disease is the Combined Health Information Database. You will need to limit your search to "Videorecording" and "kidney disease" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find video productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Videorecording (videotape, videocassette, etc.)." Type "kidney disease" (or synonyms) into the "For these words:" box. The following is a typical result when searching for video recordings on kidney disease:

- **Nutrition Connection: Guidelines for Early Kidney Disease**

  Source: Houston, TX: National Kidney Foundation of Southeast Texas. 1993.

  Contact: Available from National Kidney Foundation of Southeast Texas. 1535 West Loop, Suite 320, Houston, TX 77027. (713) 622-7440, (713) 622-8375 (FAX). PRICE: $75.

  Summary: This patient education videotape presents guidelines for the dietary management of early kidney disease. Topics include the rationale for and elements of the renal diet, suggestions for ways to increase caloric intake, and how to structure a meal plan and menu. A one-day menu is illustrated. The videotape utilizes a cartoon-like kidney-shaped character to present complex concepts in comprehensive, yet simple and interesting ways.

- **Living With Kidney Disease Then and Now**

  Source: Albuquerque, NM: IHS Kidney Disease Program and National Indian Video of America. 1996. (videocassette).

Contact: Available from Bettye Lente, IHS Kidney Disease Program. 801 Vassar Drive NE., Albuquerque, NM 87106. (505) 256-4018. PRICE: Single copy free to select health professionals working with American Indian populations.

Summary: This video is designed to help viewers recognize that many American Indians with end-stage renal disease (ESRD) live happy, productive lives. The video helps viewers feel more comfortable and confident about their choices for treatment and life as a person with kidney failure. The video opens with six American Indians expressing the feelings they had when they first learned about their ESRD. These feelings include uncertainty, denial, disappointment, anger, and frustration. The program then shows the six people successfully going about their daily lives. One young man lives in a rural area of the Navajo reservation with no running water or electricity. The program introduces him and his family, and he demonstrates how he does his exchanges at home. Two older men who both use peritoneal dialysis are shown with their families discussing how they have adjusted to life with ESRD. Another Pueblo man describes his life after receiving a kidney transplant. Two professional women are also featured. One woman is a nurse at the Zuni PHS Hospital and talks about how she copes with working and hemodialysis. The other woman is an outreach coordinator for the New Mexico Donor Program; she discusses how she manages her family, career, and peritoneal dialysis. The closing scenes focus on how the six people feel now that they are living full lives with the choices they made for treatment of their kidney disease. Feelings expressed are certainty, purpose, encouragement, hope, acceptance, and pride. (AA-M).

- **Kidney Disease**

  Source: Princeton, NJ: Films for the Humanities and Sciences. 1990.

  Contact: Available from Films for the Humanities and Sciences. P.O. Box 2053, Princeton, NJ 08543-2053. (800) 257-5126 or (609) 452-1128. PRICE: $149 (purchase), $75 (rental). Order Number FM-2364.

  Summary: This videotape deals with end-stage renal disease (ESRD), focusing on hemodialysis and organ transplantation. The video stresses that neither of these treatments is simple, painless, or inexpensive, but that both represent realistic alternatives to debilitating disease and may restore the patient to a full and normal life. The program covers the symptoms and some of the causes of kidney failure; explains how dialysis works; and covers the advantages and difficulties of kidney transplantation, including finding donor organs, tissue matching, and rejection. (AA-M).

- **Kidney Disease and Diabetes**

  Source: Los Angeles, CA: National Health Video, Inc. 2001. (videocassette).

  Contact: Available from National Health Video, Inc. 12021 Wilshire Boulevard, Suite 550, Los Angeles, CA 90025. (800) 543-6803. Fax (310) 477-8198. E-mail: healthvid@aol.com. PRICE: $89.00 plus shipping and handling.

  Summary: This videotape focuses on diabetic kidney disease. Diabetes accounts for 40 percent of all new cases of kidney failure. The stages of diabetic kidney disease are hyperfiltration, microalbuminuria, nephrotic syndrome, renal insufficiency, and end stage renal disease (ESRD). The earliest sign of kidney disease is finding small amounts of protein in the urine, so urine checks are performed regularly. If there are signs of kidney damage, more careful control of blood glucose levels and blood pressure may help. For more advanced kidney disease, a low protein diet may be recommended.

Treatment options for kidney failure are dialysis and kidney transplantation. The types of dialysis are hemodialysis and peritoneal dialysis. Transplantation is usually more effective than dialysis. The videotape is accompanied by an evaluation form and a transcript of the tape.

Audio Recordings

The Combined Health Information Database contains abstracts on audio productions. To search CHID, go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find audio productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Sound Recordings." Type "kidney disease" (or synonyms) into the "For these words:" box. The following is a typical result when searching for sound recordings on kidney disease:

- **Administering EPO: A Guide for Kidney Patients**

  Source: New York, NY: National Kidney Foundation, Inc. 1990. (audiocassette).

  Contact: Available from National Kidney Foundation, Inc. 30 East 33rd Street, New York, NY 10016. (800) 622-9010. PRICE: Single copy free.

  Summary: This audiocassette is designed for people with **kidney disease** who would like to learn about self-administration of erythropoietin (EPO). Topics in the tape include **kidney disease** and anemia; how EPO works in the treatment of anemia; how and when EPO is given; precautions regarding blood pressure, iron therapy, over-the-counter drugs, renal diet, vascular access, and dialysis prescription for patients on EPO; how EPO is made; how to administer EPO; the best injection sites; procedures for self-injection; and traveling with and storing EPO. The audiocassette is intended to be used in conjunction with written materials and with instruction from a health care provider.

- **Working Effectively with Your Dialysis Team**

  Source: Madison, WI: Life Options Rehabilitation Program. 2000. (audiocassette).

  Contact: Available from Life Options Rehabilitation Program. Medical Education Institute, Inc, 414 D'Onofrid Drive., Suite 200, Madison, WI 53719. (608) 833-8033. E-mail: lifeoptions@meiresearch.org. PRICE: Single copy free.

  Summary: This audiocassette is part of a free educational program for people with **kidney disease.** Narrated by a dialysis social worker who is on the Life Options staff, the program focuses on helping kidney patients to live active productive lives, despite the fact that they are on dialysis. The program notes that end stage renal disease (ESRD) is a life threatening illness that, for most people, means living with dialysis. The program features interviews with three patients (Harold, Jim, and Kelly), Dr. Brian Becker (a nephrologist), and Janet Shu (a dialysis clinic nurse). The narrator notes that many people feel overwhelmed by how much they have to learn and do not try because they know the dialysis team will be there to take care of the patient. But the program emphasizes that the patient is the most important member of the team and that patients who take an active part in their own care usually get better results from dialysis. The program consists of five chapters: becoming a member of the team; the other members of the health care team and what each person does; the patient's role on the health care team; communication from patients to staff; and staff communication with patients. Specific strategies are provided on how to participate in one's own health care,

recordkeeping, how to counteract depression and feeling overwhelmed by **kidney disease,** questions to ask the dialysis team (including those seemingly not related to dialysis, such as sexuality, rehabilitation, psychosocial issues), and how best to work within the framework of the dialysis unit. The program concludes with the contact information for the Life Options Rehabilitation Program (800-468-7777 or www.lifeoptions.org).

- **Handbook for Kidney Patients**

  Source: Portland, ME: National Kidney Foundation of Maine. 1990. 97 p.

  Contact: Available from National Kidney Foundation of Maine. P.O. Box 1134, Portland, ME 04104. (800) 639-7220 or (207) 772-7270. Fax (207) 772-4202. PRICE: $10.00. Also available on cassette tape and in braille.

  Summary: This patient education handbook was designed for use by persons newly diagnosed with kidney failure who are being treated at the Nephrology Associates in Portland, Maine or at the Southern Maine Dialysis Facility. Six sections cover staff and facilities; normal kidney function, **kidney disease** and dialysis; kidney transplantation and post-transplant care; diet, nutrition, exercise and medications; social work and support organizations; and a view from the patient's side, including associated feelings and emotions. Two appendices present a glossary and samples of the typical forms the patient is likely to encounter. A brief subject index is also included.

Bibliography: Multimedia on Kidney Disease

The National Library of Medicine is a rich source of information on healthcare-related multimedia productions including slides, computer software, and databases. To access the multimedia database, go to the following Web site: **http://locatorplus.gov/**. Select "Search LOCATORplus." Once in the search area, simply type in kidney disease (or synonyms). Then, in the option box provided below the search box, select "Audiovisuals and Computer Files." From there, you can choose to sort results by publication date, author, or relevance. The following multimedia has been indexed on kidney disease:

- **Kidney disease & diabetes [videorecording]** Source: NHV, National Health Video Inc; Year: 2001; Format: Videorecording; Boynton Beach, FL: Distributed by Universal Health Communications, c2001
- **Nutrition and kidney disease [videorecording]** Source: Emory University School of Medicine; Year: 1973; Format: Videorecording; Atlanta: Georgia Regional Medical Television Network: [for loan or sale by A. W. Calhoun Medical Library, 1973]
- **Polycystic kidney disease and other cystic disorders [slide]** Source: Alexander C. Chester, George E. Schreiner, Harry G. Preuss; Year: 9999; Format: Slide; [New York]: Medcom, c1978-
- **Preventable forms of kidney disease [slide]** Source: University of Michigan, Medical Center, Kidney Foundation, Michigan Dept. of Public Health; [made by] Biomedical Media Production Unit, University of Michigan, Medical Center; Year: 1978; Format: Slide; Ann Arbor: The University: [for loan or sale by its Medical Center Media Library], c1978

CHAPTER 9. PERIODICALS AND NEWS ON KIDNEY DISEASE

Overview

In this chapter, we suggest a number of news sources and present various periodicals that cover kidney disease.

News Services and Press Releases

One of the simplest ways of tracking press releases on kidney disease 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 "kidney disease" (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 kidney disease. 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 "kidney disease" (or synonyms). The following was recently listed in this archive for kidney disease:

- **New test cleared for kidney disease**
  Source: Reuters Health eLine
  Date: August 26, 2003
- **Monthly erythropoietin dosing can control anemia in kidney disease**
  Source: Reuters Medical News
  Date: November 17, 2003

- **Monthly dosing can control anemia in kidney disease**
  Source: Reuters Health eLine
  Date: November 17, 2003
- **Calcimimetic limits bone loss associated with kidney disease**
  Source: Reuters Medical News
  Date: November 14, 2003
- **Amgen drug limits bone loss from kidney disease**
  Source: Reuters Industry Breifing
  Date: November 14, 2003
- **Heart group raises alert for kidney disease patients**
  Source: Reuters Health eLine
  Date: October 30, 2003
- **AHA raises alert on cardiovascular disease risk in kidney disease patients**
  Source: Reuters Medical News
  Date: October 30, 2003
- **Risk of kidney disease progression may explain racial disparity in ESRD**
  Source: Reuters Medical News
  Date: October 24, 2003
- **Kidney disease more likely to worsen in blacks**
  Source: Reuters Health eLine
  Date: October 24, 2003
- **Young diabetics at risk for early kidney disease**
  Source: Reuters Health eLine
  Date: October 06, 2003
- **Revascularization ups survival in kidney disease patients with heart disease**
  Source: Reuters Medical News
  Date: September 18, 2003
- **Action urged on kidney disease in developing world**
  Source: Reuters Health eLine
  Date: April 15, 2003
- **Atorvastatin therapy may slow progression of chronic kidney disease**
  Source: Reuters Industry Breifing
  Date: March 19, 2003
- **Too much meat may worsen mild kidney disease**
  Source: Reuters Health eLine
  Date: March 18, 2003
- **Irbesartan reduces arterial pressure and proteinuria in pediatric kidney diseases**
  Source: Reuters Industry Breifing
  Date: January 01, 2003
- **Atherosclerosis risk factors do not predict progressive kidney disease**
  Source: Reuters Medical News
  Date: December 25, 2002
- **Treatment clues for blacks with kidney disease**
  Source: Reuters Health eLine
  Date: November 28, 2002

- **Avoid caffeine with inherited kidney disease**
  Source: Reuters Health eLine
  Date: November 07, 2002
- **Excess risk of kidney disease among blacks largely unexplained**
  Source: Reuters Medical News
  Date: September 04, 2002

The NIH

Within MEDLINEplus, the NIH has made an agreement with the New York Times Syndicate, the AP News Service, and Reuters to deliver news that can be browsed by the public. Search news releases at **http://www.nlm.nih.gov/medlineplus/alphanews_a.html**. MEDLINEplus allows you to browse across an alphabetical index. Or you can search by date at the following Web page: **http://www.nlm.nih.gov/medlineplus/newsbydate.html**. Often, news items are indexed by MEDLINEplus within its search engine.

Business Wire

Business Wire is similar to PR Newswire. To access this archive, simply go to **http://www.businesswire.com/**. You can scan the news by industry category or company name.

Market Wire

Market Wire is more focused on technology than the other wires. To browse the latest press releases by topic, such as alternative medicine, biotechnology, fitness, healthcare, legal, nutrition, and pharmaceuticals, access Market Wire's Medical/Health channel at **http://www.marketwire.com/mw/release_index?channel=MedicalHealth**. Or simply go to Market Wire's home page at **http://www.marketwire.com/mw/home**, type "kidney disease" (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 "kidney disease" (or synonyms). If you know the name of a company that is relevant to kidney disease, 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 "kidney disease" (or synonyms).

Newsletters on Kidney Disease

Find newsletters on kidney disease using the Combined Health Information Database (CHID). You will need to use the "Detailed Search" option. To access CHID, go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Limit your search to "Newsletter" and "kidney disease." Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter." Type "kidney disease" (or synonyms) into the "For these words:" box. The following list was generated using the options described above:

- **Kidney Disease? Know Your Options**

  Source: Lexington, MA: Kidney Options. 2002. 2 p.

  Contact: Available from Kidney Options. 95 Hayden Avenue, Lexington, MA 12420-9192. (866) 543-6391. Website: www.kidneyoptions.com. PRICE: Full-text available online at no charge.

  Summary: Kidney disease happens when there is damage to the filters in the kidneys. These filters remove waste products and excess fluid from the blood. There are many causes of kidney disease, including high blood pressure (hypertension) and diabetes mellitus. This newsletter briefly outlines the treatment options for people with kidney disease. Topics include hemodialysis, peritoneal dialysis, kidney transplants, the role of pre-dialysis education, social services, the importance of appropriate diet therapy, and commonly asked questions about transplants. The newsletter includes a brief profile of a transplant patient. Readers are referred to a web site (www.kidneyoptions.com) for more information.

Newsletter Articles

Use the Combined Health Information Database, and limit your search criteria to "newsletter articles." Again, you will need to use the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter Article." Type "kidney disease" (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 kidney disease:

- **Sexuality and Chronic Kidney Disease**

  Source: PKD Progress. 17(3): 5. Fall 2002.

  Contact: Available from PKD Foundation. 4901 Main Street, Suite 200, Kansas City, MO 64112-2634. (800) 753-2873. E-mail: pkdcure@pkdcure.org.

Summary: As with other chronic illnesses, the desire for sexual activity may change with the onset of kidney failure. This, of course, varies from one patient to another, but will most likely affect everyone with chronic kidney disease on some level. This brief newsletter article addresses sexuality and chronic kidney disease. The article considers the causes of reduced sexual desire, drug effects, concerns about dialysis access sites, reproduction issues, transplantation and post-transplant concerns, and strategies to cope with changes in one's sexual relationship. The author stresses that communication with one's partner and health care professional is vital in dealing with sexual dysfunction or lack of interest in sex. Kidney patients should approach these issues as they do every other aspect of kidney disease, by taking an active role in learning about the problem and treatments available.

- **From Diagnosis to Dialysis: Kidney School Helps Patients Cope with Kidney Disease**

  Source: Renal Rehabilitation Report. 10(2): S2. Summer 2002.

  Contact: Available from Life Options Rehabilitation Program. Medical Education Institute, Inc, 414 D'Onofrid Drive., Suite 200, Madison, WI 53719. (608) 833-8033. E-mail: lifeoptions@meiresearch.org.

  Summary: People affected by kidney disease encounter a wide range of emotions: sadness, anger, fear and uncertainty about the future, even depression. This brief newsletter article describes Kidney School, an online, interactive learning center that can be accessed free, 24 hours a day, at www.kidneyschool.org. Kidney School is designed to inspire, motivate, and empower people with chronic kidney disease and with kidney failure to take an active role in their health care and to improve their chances of living long and well. Kidney School consists of 16 interactive modules, addressing a wide range of topics, from exploring treatment options and anemia to vascular access care and understanding lab tests. Module 5, Coping with Kidney Disease, deals directly with the emotional aspects of kidney disease. Topics include the typical stages of adjustment, practical strategies for coping, and resources for assistance. Throughout each module, practical tips and quotes from patients help users begin to develop their own coping strategies.

- **Chronic Kidney Disease: Definition and Classification**

  Source: IHS Primary Care Provider. 27(10): 207-208. October 2002.

  Contact: Available from Indian Health Service Clinical Support Center. Two Renaissance Square, Suite 780, 40 North Central Avenue, Phoenix, AZ 85004. (602) 364-7777. Fax (602) 364-7788. E-mail: theprovider@phs.ihs.gov. Website: www.ihs.gov.

  Summary: This article describes the highlights of the National Kidney Foundation (NKF) Clinical Practice Guideline on the evaluation, classification, and stratification of chronic kidney disease (CKD). The NKF Guideline proposes a definition and classification based on a measure of kidney function, the glomerular filtration rate (GFR). The authors discuss the equations for determining GFR, normal GFR, and GFR in special populations, including children. The authors also offer brief suggestions for patient care management as GFR levels decline.

- **Pain Management in Polycystic Kidney Disease**

  Source: PKD Progress. 17(2): 12-13. Summer 2002.

  Contact: Available from PKD Foundation. 4901 Main Street, Suite 200, Kansas City, MO 64112-2634. (800) 753-2873. E-mail: pkdcure@pkdcure.org.

Summary: This article, from a newsletter for patients with polycystic kidney disease (PKD), outlines pain management strategies. The author stresses that a detailed patient history, physical examination, and examination of the urine can frequently pinpoint the cause of pain. The reasons for acute pain in the patient with PKD can differ from those that cause chronic pain. Physicians must acknowledge that the patient has pain and attempt to understand the cause of it; management of pain can then be done in a stepwise sequence. Noninvasive techniques for pain management can include ice massage, heating pads, whirlpool baths, use of the Alexander Technique, and psychobehavioral modification. The author notes that it is often difficult to cure chronic pain, but the goal is to reduce the frequency and severity of pain so as not to interfere with one's lifestyle. The next step involves analgesics (pain killers), beginning with over the counter drugs, then prescription drugs, including narcotics. If the drugs do not produce relief of pain, then more invasive techniques can be tried, such as transcutaneous electrical nerve stimulation (TENS), acupuncture, spinal cord stimulation (neuromodulation), and injection of narcotic agents directly into the spinal column. The last step is a surgical approach. The author concludes by encouraging readers not to give up hope, but to pursue a detailed evaluation and then a stepwise approach to the management of pain. The goal is to empower patients to be active participants in their own care.

- **Positive Attitude: The First Step to Living Long and Well with Kidney Disease**

  Source: Renal Rehabilitation Report. 10(2): S1, S8-S9. Summer 2002.

  Contact: Available from Life Options Rehabilitation Program. Medical Education Institute, Inc, 414 D'Onofrid Drive., Suite 200, Madison, WI 53719. (608) 833-8033. E-mail: lifeoptions@meiresearch.org.

  Summary: This newsletter article offers evidence that a positive attitude is a vital component to rebuilding a life altered by kidney disease. The author stresses that how patients view their situations has tremendous implications for how successfully they will adapt. The author outlines the 5 E's of rehabilitation: encouragement, education, exercise, employment, and evaluation. This program of 5 E's was devised in 1993 and has since by augmented by three behavioral goals: developing a positive attitude that supports active patient involvement, getting answers that can help patients self-manage effectively, and patients taking action on their own behalf. The author focuses on the importance of patients' active involvement in their own care. The author also briefly reports on research that examined the role of positive attitude and hope in a positive prognosis for people with kidney failure. To thrive at every stage of kidney disease, patients need to believe that their illness is not the end of their lives, that they are strong enough to meet the challenges, and that they can produce positive outcomes for themselves and their families. 1 figure. 14 references.

Academic Periodicals covering Kidney Disease

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to kidney disease. In addition to these sources, you can search for articles covering kidney disease that have been published by any of the periodicals listed in previous chapters. To find the latest studies published, go to **http://www.ncbi.nlm.nih.gov/pubmed**, type the name of the periodical into the search box, and click "Go."

If you want complete details about the historical contents of a journal, you can also visit the following Web site: **http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi**. Here, type in the name of the journal or its abbreviation, and you will receive an index of published articles. At **http://locatorplus.gov/**, you can retrieve more indexing information on medical periodicals (e.g. the name of the publisher). Select the button "Search LOCATORplus." Then type in the name of the journal and select the advanced search option "Journal Title Search."

CHAPTER 10. RESEARCHING MEDICATIONS

Overview

While a number of hard copy or CD-ROM resources are available for researching medications, a more flexible method is to use Internet-based databases. Broadly speaking, there are two sources of information on approved medications: public sources and private sources. We will emphasize free-to-use public sources.

U.S. Pharmacopeia

Because of historical investments by various organizations and the emergence of the Internet, it has become rather simple to learn about the medications recommended for kidney disease. 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 kidney disease. 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 kidney disease:

Acyclovir

- **Systemic - U.S. Brands:** Zovirax
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202008.html

Amantadine

- **Systemic - U.S. Brands:** Symmetrel
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202024.html

Aminoglycosides

- **Systemic - U.S. Brands:** Amikin; Garamycin; G-Mycin; Jenamicin; Kantrex; Nebcin; Netromycin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202027.html

Amlodipine

- **Systemic - U.S. Brands:** Norvasc
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202670.html

Amphotericin B

- **Systemic - U.S. Brands:** Amphocin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202032.html

Angiotensin-Converting Enzyme (Ace) Inhibitors

- **Systemic - U.S. Brands:** Accupril; Aceon; Altace; Capoten; Lotensin; Mavik; Monopril; Prinivil; Univasc; Vasotec 4; Zestril
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202044.html

Angiotensin-Converting Enzyme (Ace) Inhibitors and Hydrochlorothiazide

- **Systemic - U.S. Brands:** Accuretic; Capozide; Lotensin HCT; Prinzide; Uniretic; Vaseretic; Zestoretic
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202045.html

Antidiabetic Agents, Sulfonylurea

- **Systemic - U.S. Brands:** Amaryl; DiaBeta; Diabinese; Dymelor; Glucotrol; Glucotrol XL; Glynase PresTab; Micronase; Orinase; Tolinase
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202742.html

Antifungals, Azole

- **Systemic - U.S. Brands:** Diflucan; Nizoral; Sporanox
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202697.html

Aztreonam

- **Systemic - U.S. Brands:** Azactam
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202078.html

Beta-Adrenergic Blocking Agents

- **Systemic - U.S. Brands:** Betapace; Blocadren; Cartrol; Corgard; Inderal; Inderal LA; Kerlone; Levatol; Lopressor; Normodyne; Sectral; Tenormin; Toprol-XL; Trandate; Visken; Zebeta
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202087.html

Beta-Adrenergic Blocking Agents and Thiazide Diuretics

- **Systemic - U.S. Brands:** Corzide 40/5; Corzide 80/5; Inderide; Inderide LA; Lopressor HCT; Tenoretic 100; Tenoretic 50; Timolide 10-25; Ziac
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202088.html

Calcium Acetate

- **Systemic - U.S. Brands:** PhosLo
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203481.html

Calcium Channel Blocking Agents

- **Systemic - U.S. Brands:** Adalat; Adalat CC; Calan; Calan SR; Cardene; Cardizem; Cardizem CD; Cardizem SR; Dilacor-XR; DynaCirc; Isoptin; Isoptin SR; Nimotop; Plendil; Procardia; Procardia XL; Vascor; Verelan
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202107.html

Cephalosporins

- **Systemic - U.S. Brands:** Ancef; Ceclor; Ceclor CD; Cedax; Cefadyl; Cefizox; Cefobid; Cefotan; Ceftin; Cefzil; Ceptaz; Claforan; Duricef; Fortaz; Keflex 20; Keftab 20; Kefurox; Kefzol; Mandol; Maxipime; Mefoxin; Monocid; Omnicef; Rocephin; Suprax; Tazicef; Tazidime; Vantin; Velo
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202119.html

Chlorambucil

- **Systemic - U.S. Brands:** Leukeran
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202124.html

Cinoxacin

- **Systemic - U.S. Brands:** Cinobac
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202141.html

Clarithromycin

- **Systemic - U.S. Brands:** Biaxin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202667.html

Clonidine

- **Systemic - U.S. Brands:** Catapres; Catapres-TTS
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202152.html

Clonidine and Chlorthalidone

- **Systemic - U.S. Brands:** Combipres
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202153.html

Copper Supplements

- **Systemic - U.S. Brands:** Note:
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202164.html

Cyclophosphamide

- **Systemic - U.S. Brands:** Cytoxan; Neosar
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202174.html

Diuretics, Loop

- **Systemic - U.S. Brands:** Bumex; Edecrin; Lasix; Myrosemide
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202205.html

Diuretics, Potassium-Sparing

- **Systemic - U.S. Brands:** Aldactone; Dyrenium; Midamor
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202206.html

Diuretics, Potassium-Sparing, and Hydrochlorothiazide

- **Systemic - U.S. Brands:** Aldactazide; Dyazide; Maxzide; Moduretic; Spirozide
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202207.html

Diuretics, Thiazide

- **Systemic - U.S. Brands:** Aquatensen; Diucardin; Diulo; Diuril; Enduron; Esidrix; Hydro-chlor; Hydro-D; HydroDIURIL; Hydromox; Hygroton; Metahydrin; Microzide; Mykrox; Naqua; Naturetin; Oretic; Renese; Saluron; Thalitone; Trichlorex 10; Zaroxolyn
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202208.html

Doxazosin

- **Systemic - U.S. Brands:** Cardura
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202629.html

Epoetin

- **Systemic - U.S. Brands:** Epogen; Procrit
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202214.html

Famciclovir

- **Systemic - U.S. Brands:** Famvir
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202723.html

Fludrocortisone

- **Systemic - U.S. Brands:** Florinef
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202244.html

Fluoroquinolones

- **Systemic - U.S. Brands:** Avelox; Cipro; Cipro I.V.; Floxin; Floxin I.V.; Levaquin; Maxaquin; Noroxin; Penetrex; Tequin; Zagam
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202656.html

Growth Hormone

- **Systemic - U.S. Brands:** Genotropin; Genotropin Miniquick; Humatrope; Norditropin; Nutropin; Nutropin AQ; Protropin; Saizen; Serostim
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202269.html

Guanabenz

- **Systemic - U.S. Brands:** Wytensin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202271.html

Guanadrel

- **Systemic - U.S. Brands:** Hylorel
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202272.html

Guanethidine

- **Systemic - U.S. Brands:** Ismelin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202273.html

Guanfacine

- **Systemic - U.S. Brands:** Tenex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202275.html

Hepatitis B Vaccine Recombinant

- **Systemic - U.S. Brands:** Engerix-B
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202281.html

Hydralazine and Hydrochlorothiazide

- **Systemic - U.S. Brands:** Apresazide
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202286.html

Indapamide

- **Systemic - U.S. Brands:** Lozol
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202296.html

Insulin

- **Systemic - U.S. Brands:** Humulin 50/50; Humulin 70/30; Humulin 70/30 Pen; Humulin L; Humulin N; Humulin N Pen; Humulin R; Humulin R, Regular U-500 (Concentrated); Humulin U; Lente; Lente Iletin II; Novolin 70/30; Novolin 70/30 PenFill; Novolin 70/30 Prefilled; Novolin L; Novoli
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203298.html

Lamivudine

- **Systemic - U.S. Brands:** Epivir; Epivir-HBV
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202292.html
- **Systemic - U.S. Brands:** Epivir; Epivir-HBV
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202791.html
- **Systemic - U.S. Brands:** Epivir; Epivir-HBV
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203689.html

Levocarnitine

- **Systemic - U.S. Brands:** Carnitor
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202325.html

Loracarbef

- **Systemic - U.S. Brands:** Lorabid
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202680.html

Losartan

- **Systemic - U.S. Brands:** Cozaar
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202767.html

Losartan and Hydrochlorothiazide

- **Systemic - U.S. Brands:** Hyzaar
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203639.html

Mecamylamine

- **Systemic - U.S. Brands:** Inversine
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202340.html

Metformin

- **Systemic - U.S. Brands:** Glucophage
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202756.html

Methyldopa

- **Systemic - U.S. Brands:** Aldomet
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202359.html

Methyldopa and Thiazide Diuretics

- **Systemic - U.S. Brands:** Aldoclor; Aldoril
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202360.html

Minoxidil

- **Systemic - U.S. Brands:** Loniten
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202373.html

Nateglinide

- **Systemic - U.S. Brands:** Starlix
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500277.html

Prazosin

- **Systemic - U.S. Brands:** Minipress
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202475.html

Prazosin and Polythiazide

- **Systemic - U.S. Brands:** Minizide
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202476.html

Rauwolfia Alkaloids

- **Systemic - U.S. Brands:** Harmonyl; Raudixin; Rauval; Rauverid; Serpalan; Wolfina
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202503.html

Rauwolfia Alkaloids and Thiazide Diuretics

- **Systemic - U.S. Brands:** Demi-Regroton; Diupres; Diurigen with Reserpine; Diutensen-R; Enduronyl; Enduronyl Forte; Oreticyl; Oreticyl Forte; Rauzide; Regroton
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202504.html

Reserpine, Hydralazine, and Hydrochlorothiazide

- **Systemic - U.S. Brands:** Cam-Ap-Es; Cherapas; Ser-A-Gen; Seralazide; Ser-Ap-Es; Serpazide; Tri-Hydroserpine; Unipres
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202506.html

Rimantadine

- **Systemic - U.S. Brands:** Flumadine
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202771.html

Sevelamer

- **Oral - U.S. Brands:** Renagel
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203741.html

Stavudine

- **Systemic - U.S. Brands:** Zerit
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202728.html

Sulfonamides and Phenazopyridine

- **Systemic - U.S. Brands:** Azo Gantanol; Azo Gantrisin; Azo-Sulfamethoxazole; Azo-Sulfisoxazole; Azo-Truxazole; Sul-Azo
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202542.html

Terazosin

- **Systemic - U.S. Brands:** Hytrin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202546.html

Torsemide

- **Systemic - U.S. Brands:** Demadex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202740.html

Trimethoprim

- **Systemic - U.S. Brands:** Proloprim; Trimpex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202579.html

Valacyclovir

- **Systemic - U.S. Brands:** Valtrex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202790.html

Vitamin B 12

- **Systemic - U.S. Brands:** Alphamin; Cobex; Cobolin-M; Crystamine; Crysti-12; Cyanoject; Cyomin; Hydrobexan; Hydro-Cobex; Hydro-Crysti-12; Hydroxy-Cobal; LA-12; Nascobal; Neuroforte-R; Primabalt; Rubramin PC; Shovite; Vibal; Vibal LA; Vitabee 12
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202596.html

Vitamin D and Related Compounds

- **Systemic - U.S. Brands:** Calciferol; Calciferol Drops; Calcijex; Calderol; DHT; DHT Intensol; Drisdol; Drisdol Drops; Hectorol; Hytakerol; Rocaltrol; Zemplar
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202597.html

Zalcitabine

- **Systemic - U.S. Brands:** HIVID
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202652.html

Zinc Supplements

- **Systemic - U.S. Brands:** Orazinc; Verazinc; Zinc 15; Zinc-220; Zinca-Pak; Zincate
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202622.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[13]:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://www.cancer.gov/cancerinfo/list.aspx?viewid=5f35036e-5497-4d86-8c2c-714a9f7c8d25**
- National Eye Institute (NEI); guidelines available at **http://www.nei.nih.gov/order/index.htm**
- National Heart, Lung, and Blood Institute (NHLBI); guidelines available at **http://www.nhlbi.nih.gov/guidelines/index.htm**
- National Human Genome Research Institute (NHGRI); research available at **http://www.genome.gov/page.cfm?pageID=10000375**
- National Institute on Aging (NIA); guidelines available at **http://www.nia.nih.gov/health/**

[13] These publications are typically written by one or more of the various NIH Institutes.

- National Institute on Alcohol Abuse and Alcoholism (NIAAA); guidelines available at **http://www.niaaa.nih.gov/publications/publications.htm**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); fact sheets and guidelines available at **http://www.niams.nih.gov/hi/index.htm**
- National Institute of Child Health and Human Development (NICHD); guidelines available at **http://www.nichd.nih.gov/publications/pubskey.cfm**
- National Institute on Deafness and Other Communication Disorders (NIDCD); fact sheets and guidelines at **http://www.nidcd.nih.gov/health/**
- National Institute of Dental and Craniofacial Research (NIDCR); guidelines available at **http://www.nidr.nih.gov/health/**
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); guidelines available at **http://www.niddk.nih.gov/health/health.htm**
- National Institute on Drug Abuse (NIDA); guidelines available at **http://www.nida.nih.gov/DrugAbuse.html**
- National Institute of Environmental Health Sciences (NIEHS); environmental health information available at **http://www.niehs.nih.gov/external/facts.htm**
- National Institute of Mental Health (NIMH); guidelines available at **http://www.nimh.nih.gov/practitioners/index.cfm**
- National Institute of Neurological Disorders and Stroke (NINDS); neurological disorder information pages available at **http://www.ninds.nih.gov/health_and_medical/disorder_index.htm**
- National Institute of Nursing Research (NINR); publications on selected illnesses at **http://www.nih.gov/ninr/news-info/publications.html**
- National Institute of Biomedical Imaging and Bioengineering; general information at **http://grants.nih.gov/grants/becon/becon_info.htm**
- Center for Information Technology (CIT); referrals to other agencies based on keyword searches available at **http://kb.nih.gov/www_query_main.asp**
- National Center for Complementary and Alternative Medicine (NCCAM); health information available at **http://nccam.nih.gov/health/**
- National Center for Research Resources (NCRR); various information directories available at **http://www.ncrr.nih.gov/publications.asp**
- Office of Rare Diseases; various fact sheets available at **http://rarediseases.info.nih.gov/html/resources/rep_pubs.html**
- Centers for Disease Control and Prevention; various fact sheets on infectious diseases available at **http://www.cdc.gov/publications.htm**

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[14] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full-text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[15]

- **Bioethics:** Access to published literature on the ethical, legal, and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to cancer-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**

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[14] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[15] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

The Combined Health Information Database

A comprehensive source of information on clinical guidelines written for professionals is the Combined Health Information Database. You will need to limit your search to one of the following: Brochure/Pamphlet, Fact Sheet, or Information Package, and "kidney disease" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For the publication date, select "All Years." Select your preferred language and the format option "Fact Sheet." Type "kidney disease" (or synonyms) into the "For these words:" box. The following is a sample result:

- **Diet for Patients With Kidney Disease**

  Source: Sparks, MD: Maryland Dietetic Association. 1990. 28 p.

  Contact: Available from Maryland Dietetic Association. Attn: Helen Mullan, 18 Far Corners Loop, Sparks, MD 21152. (410) 955-6343. PRICE: $3 plus $1.50 shipping and handling. Bulk prices available.

  Summary: The booklet discusses the renal diet in general, provides blank spaces for individualizing the material, and covers topics including tips for eating out, using seasonings, high sodium foods, high potassium foods, and high phosphorus foods. The booklet has removable pages, which the educator may add or delete as desired, depending on diet prescription. The information packet also includes copies of the individual sheets available separately from the booklet (covering the same topics). All materials are written at a 6th to 7th grade reading level.

- **Blood Pressure Control in Individuals with Pre-Kidney Disease**

  Source: in Exceptional Parent. End Stage Renal Disease: A Practical Guide for Physicians, Dietitians, Nurses, Patients, Families, and Caregivers. Englewood Cliffs, NJ: Exceptional Parent. 1999. p. 7-8.

  Contact: Available from Exceptional Parent. P.O. Box 1807, Englewood Cliffs, NJ 07632. (800) 535-1910. Fax (201) 947-9376. E-mail: eplibrary@aol.com. Website: www.eparent.com. PRICE: $5.95.

  Summary: This article is from a monograph written to soften the blow of receiving the diagnosis of kidney failure by providing patients, caregivers, and their families some practical, easy to read information. The articles are written to be practical enough for patients to use, yet informative enough that professionals can refer to them as well. This article considers the role of blood pressure control in individuals with kidney disease. The author first reviews blood pressure, how it is measured, and the complications associated with high blood pressure (hypertension). The author then explains how high blood pressure affects the kidneys; years of untreated or poorly controlled blood pressure lead to irreversible scarring of the kidney, ending in kidney failure, dialysis,

and the need for a kidney transplant. Under normal circumstances, the kidney has a unique ability to automatically regulate its own pressure. However, if blood pressure stays high over long periods of time, this autoregulatory function of the kidney is slowly destroyed, and renal circulation begins to suffer. The author discusses the use of a continuum for measuring blood pressure, noting that optimal blood pressure is a systolic reading of less than 120 with a diastolic reading of less than 80. In general, blood pressure should be kept well below 140 over 90. Individuals with diabetes or symptoms of abnormal kidney function, however, must keep their blood pressure below 135 over 85 for maximal protection against further kidney injury. These patients need to be aware of this goal and should work with their physicians to try to achieve it, knowing that in more than half the cases at least two different antihypertensive medications will be needed. 1 figure. 1 table.

- **Role of Diet in the Treatment of Kidney Disease**

  Source: in Exceptional Parent. End Stage Renal Disease: A Practical Guide for Physicians, Dietitians, Nurses, Patients, Families, and Caregivers. Englewood Cliffs, NJ: Exceptional Parent. 1999. p. 9.

  Contact: Available from Exceptional Parent. P.O. Box 1807, Englewood Cliffs, NJ 07632. (800) 535-1910. Fax (201) 947-9376. E-mail: eplibrary@aol.com. Website: www.eparent.com. PRICE: $5.95.

  Summary: This brief article on the role of diet is from a monograph written to soften the blow of receiving the diagnosis of kidney failure by providing patients, caregivers, and their families some practical, easy to read information. The articles are written to be practical enough for patients to use, yet informative enough that professionals can refer to them as well. This article recommends that any individual with kidney disease (either chronic kidney failure or end stage renal disease, ESRD) be referred to a renal dietitian for nutrition consultation. The renal dietitian will perform a complete nutrition assessment that includes a review of the individual's medical, surgical, and diet histories, blood tests, and medications. After the information is collected and reviewed, the dietitian develops a nutritional care plan with objectives and goals. The care plan includes nutrient requirements, such as the amount of protein and calories that the person needs to maintain a good nutritional status. The author notes that the ability to incorporate cultural foods, practices, and preferences in the dietary plan is important for dietary compliance. Whatever the belief and practice, every diet plan needs to be individualized for the person who must follow it. The article includes the toll free number of the National Kidney Foundation (800 622 9010) through which readers can locate a renal dietitian.

The NLM Gateway[16]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface, providing one-stop searching for many of NLM's information resources or databases.[17] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**.

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[16] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

[17] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

Type "kidney disease" (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	255101
Books / Periodicals / Audio Visual	1798
Consumer Health	1390
Meeting Abstracts	99
Other Collections	5
Total	258393

HSTAT[18]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[19] These documents include clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[20] Simply search by "kidney disease" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

Coffee Break: Tutorials for Biologists[21]

Coffee Break is a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. Here you will find a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[22] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[23] This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for

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[18] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.

[19] The HSTAT URL is **http://hstat.nlm.nih.gov/**.

[20] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services' *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.

[21] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

[22] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[23] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

The Genome Project and Kidney Disease

In the following section, we will discuss databases and references which relate to the Genome Project and kidney disease.

Online Mendelian Inheritance in Man (OMIM)

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).[24] The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

To search the database, go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html**. Type "kidney disease" (or synonyms) into the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. In particular, the option "Database Links" will search across technical databases that offer an abundance of information. The following is an example of the results you can obtain from the OMIM for kidney disease:

- **Cystic Kidney Disease with Ventriculomegaly**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?219730
- **Glomerulocystic Kidney Disease, Hypoplastic Type**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?137920
- **Medullary Cystic Kidney Disease 1**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?174000
- **Medullary Cystic Kidney Disease 2**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?603860

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[24] Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

- **Polycystic Kidney Disease 1**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?601313
- **Polycystic Kidney Disease 2**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?173910
- **Polycystic Kidney Disease 3, Autosomal Dominant**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?600666
- **Polycystic Kidney Disease and Sea Urchin Rej Homolog-like**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?604670
- **Polycystic Kidney Disease, Autosomal Recessive**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?263200
- **Polycystic Kidney Disease, Infantile Severe, with Tuberous Sclerosis**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?600273
- **Polycystic Kidney Disease, Potter Type I, with Microbrachycephaly, Hypertelorism, and Brachymelia**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?263210

Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web site categorizes each disorder by system of the body. Go to **http://www.ncbi.nlm.nih.gov/disease/**, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to revisit it from time to time. The following systems and associated disorders are addressed:

- **Cancer:** Uncontrolled cell division.
  Examples: Breast and ovarian cancer, Burkitt lymphoma, chronic myeloid leukemia, colon cancer, lung cancer, malignant melanoma, multiple endocrine neoplasia, neurofibromatosis, p53 tumor suppressor, pancreatic cancer, prostate cancer, Ras oncogene, RB: retinoblastoma, von Hippel-Lindau syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Cancer.html**
- **Immune System:** Fights invaders.
  Examples: Asthma, autoimmune polyglandular syndrome, Crohn's disease, DiGeorge syndrome, familial Mediterranean fever, immunodeficiency with Hyper-IgM, severe combined immunodeficiency.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Immune.html**
- **Metabolism:** Food and energy.
  Examples: Adreno-leukodystrophy, atherosclerosis, Best disease, Gaucher disease, glucose galactose malabsorption, gyrate atrophy, juvenile-onset diabetes, obesity, paroxysmal nocturnal hemoglobinuria, phenylketonuria, Refsum disease, Tangier disease, Tay-Sachs disease.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Metabolism.html**
- **Muscle and Bone:** Movement and growth.
  Examples: Duchenne muscular dystrophy, Ellis-van Creveld syndrome, Marfan syndrome, myotonic dystrophy, spinal muscular atrophy.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Muscle.html**

- **Nervous System:** Mind and body.
  Examples: Alzheimer disease, amyotrophic lateral sclerosis, Angelman syndrome, Charcot-Marie-Tooth disease, epilepsy, essential tremor, fragile X syndrome, Friedreich's ataxia, Huntington disease, Niemann-Pick disease, Parkinson disease, Prader-Willi syndrome, Rett syndrome, spinocerebellar atrophy, Williams syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Brain.html**
- **Signals:** Cellular messages.
  Examples: Ataxia telangiectasia, Cockayne syndrome, glaucoma, male-patterned baldness, SRY: sex determination, tuberous sclerosis, Waardenburg syndrome, Werner syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Signals.html**
- **Transporters:** Pumps and channels.
  Examples: Cystic fibrosis, deafness, diastrophic dysplasia, Hemophilia A, long-QT syndrome, Menkes syndrome, Pendred syndrome, polycystic kidney disease, sickle cell anemia, Wilson's disease, Zellweger syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Transporters.html**

Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **3D Domains:** Domains from Entrez Structure,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Books:** Online books,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books**
- **Genome:** Complete genome assemblies,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome**
- **NCBI's Protein Sequence Information Survey Results:**
  Web site: **http://www.ncbi.nlm.nih.gov/About/proteinsurvey/**
- **Nucleotide Sequence Database (Genbank):**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide**
- **OMIM:** Online Mendelian Inheritance in Man,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**
- **PopSet:** Population study data sets,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset**
- **ProbeSet:** Gene Expression Omnibus (GEO),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Protein Sequence Database:**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein**
- **PubMed:** Biomedical literature (PubMed),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed**

- **Structure:** Three-dimensional macromolecular structures,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure**
- **Taxonomy:** Organisms in GenBank,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy**

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=genome**, and then select the database that you would like to search. The databases available are listed in the drop box next to "Search." Enter "kidney disease" (or synonyms) into the search box and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[25]

This online resource has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually limited or completely omitted in existing reference sources due to space limitations of the printed form.

At **http://www.nlm.nih.gov/mesh/jablonski/syndrome_toc/toc_a.html**, you can search across syndromes using an alphabetical index**.** Search by keywords at **http://www.nlm.nih.gov/mesh/jablonski/syndrome_db.html**.

The Genome Database[26]

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type "kidney disease" (or synonyms) into the search box,

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[25] Adapted from the National Library of Medicine: **http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html**.

[26] Adapted from the Genome Database: **http://gdbwww.gdb.org/gdb/aboutGDB.html - mission**.

and review the results. If more than one word is used in the search box, then separate each one with the word “and” or “or” (using “or” might be useful when using synonyms).

APPENDIX B. PATIENT RESOURCES

Overview

Official agencies, as well as federally funded institutions supported by national grants, frequently publish a variety of guidelines written with the patient in mind. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. Since new guidelines on kidney disease 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 kidney disease. 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 kidney disease. 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 "kidney disease":

- Other guides

  Diabetic Kidney Problems
  http://www.nlm.nih.gov/medlineplus/diabetickidneyproblems.html

  Kidney Diseases
  http://www.nlm.nih.gov/medlineplus/kidneydiseases.html

  Kidney Failure and Dialysis
  http://www.nlm.nih.gov/medlineplus/kidneyfailureanddialysis.html

  Kidney Stones
  http://www.nlm.nih.gov/medlineplus/kidneystones.html

  Kidney Transplantation
  http://www.nlm.nih.gov/medlineplus/kidneytransplantation.html

Within the health topic page dedicated to kidney disease, the following was listed:

- General/Overviews

  Kidney and Urinary Tract Function, Disorders, and Diseases
  Source: American Association for Clinical Chemistry
  http://www.labtestsonline.org/understanding/conditions/kidney.html

  Kidney Diseases
  http://www.4woman.gov/faq/Easyread/kidney-etr.htm

  Kidney School
  Source: Life Options Rehabilitation Program
  http://www.kidneyschool.org/

- Diagnosis/Symptoms

  24-Hour Urine Collection
  Source: National Institutes of Health, Clinical Center
  http://www.cc.nih.gov/ccc/patient_education/procdiag/24hr.pdf

  Albumin Test
  Source: American Association for Clinical Chemistry
  http://www.labtestsonline.org/understanding/analytes/albumin/test.html

  Calcium Test
  Source: American Association for Clinical Chemistry
  http://www.labtestsonline.org/understanding/analytes/calcium/test.html

  Cystoscopy and Ureteroscopy
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/cystoscopy/index.htm

  Glomerular Filtration Rate (GFR)
  Source: National Institutes of Health, Clinical Center
  http://www.cc.nih.gov/ccc/patient_education/procdiag/glomerular.pdf

  Hematuria (Blood in the Urine)
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/hematuria/index.htm

Intravenous Pyelogram
http://www.nlm.nih.gov/medlineplus/tutorials/ivploader.html

Intravenous Pyelogram (IVP)
Source: National Institutes of Health, Clinical Center
http://www.cc.nih.gov/ccc/patient_education/procdiag/ivp.pdf

Kidney Biopsy
Source: National Kidney and Urologic Diseases Information Clearinghouse
http://kidney.niddk.nih.gov/kudiseases/pubs/biopsy/index.htm

Magnesium Test
Source: American Association for Clinical Chemistry
http://www.labtestsonline.org/understanding/analytes/magnesium/test.html

Microalbumin
Source: American Association for Clinical Chemistry
http://www.labtestsonline.org/understanding/analytes/microalbumin/test.html

Ultrasound-Abdomen
Source: American College of Radiology, Radiological Society of North America
http://www.radiologyinfo.org/content/ultrasound-abdomen.htm

- Treatment

  Angiotensin Receptor Blockers
  http://circ.ahajournals.org/cgi/reprint/107/24/e215.pdf

- Specific Conditions/Aspects

  Analgesic Nephropathy (Painkillers and the Kidneys)
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/analgesicnephropathy/index.htm

  Genital and Urinary Tract Defects
  Source: March of Dimes Birth Defects Foundation
  http://www.marchofdimes.com/professionals/681_1215.asp

  Glomerular Diseases
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/glomerular/index.htm

  Glomerular Diseases
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/glomerular/index.htm??

  Goodpasture's Syndrome
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/goodpasture/index.htm

  High Blood Pressure and Kidney Disease
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/highblood/index.htm

  IgA Nephropathy
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/iganephropathy/index.htm

Ischemic Nephropathy
Source: Mayo Foundation for Medical Education and Research
http://www.mayoclinic.com/invoke.cfm?id=AN00297

Kidney Failure and Cardiovascular Disease
http://circ.ahajournals.org/cgi/reprint/108/16/e114.pdf

Kidney Ptosis
Source: Mayo Foundation for Medical Education and Research
http://www.mayoclinic.com/invoke.cfm?id=AN00383

Lupus Nephritis
Source: National Kidney and Urologic Diseases Information Clearinghouse
http://kidney.niddk.nih.gov/kudiseases/pubs/lupusnephritis/index.htm

Medullary Sponge Kidney
Source: Mayo Foundation for Medical Education and Research
http://www.mayoclinic.com/invoke.cfm?id=AN00343

Multicystic Kidney Dysplasia
Source: Mayo Foundation for Medical Education and Research
http://www.mayoclinic.com/invoke.cfm?id=AN00565

Nephrotic Syndrome in Adults
Source: National Kidney and Urologic Diseases Information Clearinghouse
http://kidney.niddk.nih.gov/kudiseases/pubs/nephrotic/index.htm

Post-Infectious Glomerulonephritis
Source: Mayo Foundation for Medical Education and Research
http://www.mayoclinic.com/invoke.cfm?id=AN00629

Proteinuria
Source: National Kidney and Urologic Diseases Information Clearinghouse
http://kidney.niddk.nih.gov/kudiseases/pubs/proteinuria/index.htm

Pyelonephritis (Kidney Infection) in Adults
Source: National Kidney and Urologic Diseases Information Clearinghouse
http://kidney.niddk.nih.gov/kudiseases/pubs/pyelonephritis/index.htm

Renal Osteodystrophy
Source: National Kidney and Urologic Diseases Information Clearinghouse
http://kidney.niddk.nih.gov/kudiseases/pubs/renalosteodystrophy/index.htm

Renal Tubular Acidosis
Source: National Kidney and Urologic Diseases Information Clearinghouse
http://kidney.niddk.nih.gov/kudiseases/pubs/tubularacidosis/index.htm

Shrinking Kidney
Source: Mayo Foundation for Medical Education and Research
http://www.mayoclinic.com/invoke.cfm?id=AN00408

Simple Kidney Cysts
Source: National Kidney and Urologic Diseases Information Clearinghouse
http://kidney.niddk.nih.gov/kudiseases/pubs/cysts/index.htm

Single Kidney
Source: Mayo Foundation for Medical Education and Research
http://www.mayoclinic.com/invoke.cfm?id=AN00047

- Children

  Childhood Nephrotic Syndrome
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/childhoodnephrotic/index.htm

  Hemolytic Uremic Syndrome
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/hemolyticuremic/index.htm

  Kidney Diseases in Childhood
  Source: Nemours Foundation
  http://kidshealth.org/parent/medical/kidney/kidney_diseases_childhood.html

  Vesicoureteral Reflux
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/vesicoureteralreflux/index.htm

  When Your Child Has a Chronic Kidney Disease
  Source: Nemours Foundation
  http://kidshealth.org/parent/medical/kidney/chronic_kidney_disease.html

- From the National Institutes of Health

  Kidney and Urologic Diseases
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/index.asp

- Journals/Newsletter

  E-Kidney: Online Newsletter of the NKF
  Source: National Kidney Foundation
  http://www.kidney.org/general/eleckid/

  Renal Flash
  Source: American Association of Kidney Patients
  http://www.aakp.org/Renal_Flash_Issues.htm

- Latest News

  Low-Dose Aspirin May Affect Kidneys in Elderly
  Source: 11/06/2003, Reuters Health
  http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory_14556.html

  New Statement Says People with Kidney Disease Are at Highest Risk for Heart Disease
  Source: 10/28/2003, American Heart Association
  http://www.americanheart.org/presenter.jhtml?identifier=3016382

- Men

  Pregnancy and Kidney Disease
  Source: National Kidney Foundation
  http://www.kidney.org/general/atoz/content/pregnancy.html

- Organizations

  American Association of Kidney Patients
  http://www.aakp.org/

  American Kidney Fund
  http://www.akfinc.org/

  National Institute of Diabetes and Digestive and Kidney Diseases
  http://www.niddk.nih.gov/

  National Kidney and Urologic Diseases Information Clearinghouse
  Source: National Institute of Diabetes and Digestive and Kidney Diseases
  http://kidney.niddk.nih.gov/

  National Kidney Foundation
  http://www.kidney.org/

  Polycystic Kidney Research Foundation
  http://www.pkdcure.org/

- Prevention/Screening

  You Have the Power to Prevent Kidney Disease: Learn the Risks
  http://www.nkdep.nih.gov/pdf/nkdep_brochure.pdf

- Research

  New Technology for Kidney Surgery Leads to Same Outcome
  Source: American Cancer Society
  http://www.cancer.org/docroot/nws/content/nws_1_1x_new_technology_for_kidney_surgery_leads_to_same_outcome.asp

  Rigorous, Short-Term Diet-Exercise Program Lowers Heart Disease Risk
  Source: American Heart Association
  http://www.americanheart.org/presenter.jhtml?identifier=3005952

- Statistics

  FASTATS: Kidney/Bladder Disorders
  Source: National Center for Health Statistics
  http://www.cdc.gov/nchs/fastats/kidbladd.htm

  Kidney and Urologic Disease Statistics for the United States
  Source: National Kidney and Urologic Diseases Information Clearinghouse
  http://kidney.niddk.nih.gov/kudiseases/pubs/kustats/index.htm

- Teenagers

  Chronic Kidney Conditions
  Source: Nemours Foundation
  http://kidshealth.org/teen/diseases_conditions/urinary/kidney.html

  Kidneys and Urinary Tract
  Source: Nemours Foundation
  http://kidshealth.org/teen/your_body/body_basics/kidneys.html

- Women

  Pregnancy and Kidney Disease
  Source: National Kidney Foundation
  http://www.kidney.org/general/atoz/content/pregnancy.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 kidney disease. 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:

- **Anemia in Kidney Disease and Dialysis**

  Source: Bethesda, MD: National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH). 2001. 4 p.

  Contact: Available from National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). 3 Information Way, Bethesda, MD 20892-3580. (800) 891-5390 or (301) 654-4415. Fax (301)634-0716. E-mail: nkudic@info.niddk.nih.gov. Website: www.niddk.nih.gov/health/kidney/nkudic.htm PRICE: Full-text available online at no charge; single copy free; bulk orders available. Order number: KU-146.

  Summary: Anemia (low levels of red blood cells) is common in people with kidney disease. Healthy kidneys produce a hormone called erythropoietin (EPO) which stimulates the bone marrow to produce the proper number of red blood cells needed to carry oxygen to vital organs. Diseased kidneys, however, often do not make enough EPO. Other common causes of anemia include loss of blood from hemodialysis and low levels of iron and folic acid. This fact sheet describes anemia in kidney disease and dialysis. The presence of anemia is determined by a complete blood count (CBC), which includes a determination of hematocrit (Hct) level, which is the percentage of the blood that consists of red blood cells. Anemia can begin with chronic renal insufficiency, and tends to worsen as kidney disease progresses. Treatment includes EPO injections, and iron supplements; a few people may also need vitamin B12 and folic acid supplements to keep anemia under control and let patients feel better, live longer, and have more energy. The fact sheet concludes with a description of current research projects in this area, a brief list of resource organizations for more information, and a brief description of the National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC) and its contact information. 2 figures. 1 table.

- **What You Need to Know About Anemia and Chronic Kidney Disease**

  Source: New York, NY: National Kidney Foundation (NKF). 2002. 7 p.

  Contact: Available from National Kidney Foundation (NKF). 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Website: www.kidney.org. PRICE: Single copy free.

  Summary: Anemia occurs when the red blood cells in the body are in short supply. Red blood cells carry oxygen from the lungs to all the organs and tissues, providing energy for daily activities. This brochure reviews the interplay of anemia and chronic kidney disease. The brochure describes the symptoms of anemia, its causes, why chronic kidney disease causes anemia, treatment options, the indications for dietary supplements to help treat anemia, other dietary changes that may be helpful, and complications of untreated anemia. One sidebar offers suggestions for questions to ask the health care provider about anemia. Chronic kidney disease may cause anemia because of a low level of the hormone called erythropoietin (EPO) which stimulates red blood cell production. In chronic kidney disease, iron supplements are often needed along with EPO to treat anemia. The brochure includes a brief description of the work and publications of the National Kidney Foundation (NKF, www.kidney.org).

- **Pediatric ESRD Fact Sheet: Chronic Kidney Disease**

  Source: Pitman, NJ: American Nephrology Nurses' Association. 2003. 4 p.

  Contact: Available from American Nephrology Nurses' Association. East Holly Avenue, Box 56, Pitman, NJ 08071. (856) 256-2320 or (888) 600-2662. Website: www.annanurse.org. PRICE: Single copy free.

  Summary: Chronic kidney disease (CKD) may occur as a result of many systemic disorders or congenital malformations. Children with CKD may experience fatigue, sluggishness, decreased urine output, anemia, bone disease, and hypertension (high blood pressure). The treatment involves the use of medications, special diet, and dialysis or transplantation. This brochure educates teachers about CKD, particularly as it may apply to a student in their classroom, focusing on the common signs and symptoms of the disease. The brochure describes common medications used in treatment and nutritional considerations. The brochure includes space for the nephrology nurse's telephone number, for the teacher to contact with any questions.

- **Diabetes and Chronic Kidney Disease: A Guide for American Indians and Alaska Natives**

  Source: New York, NY: National Kidney Foundation (NKF). 2002. 11 p.

  Contact: Available from National Kidney Foundation (NKF). 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Website: www.kidney.org. PRICE: Single copy free.

  Summary: Diabetes is the number one cause of chronic kidney disease (diabetic nephropathy) and other serious health problems like heart disease (angiopathy), eye disease (diabetic retinopathy) and nerve damage (diabetic neuropathy). One out of vie American Indians and Alaska Natives has diabetes, compared with one of 20 adults in the general United States population. This brochure reviews the interplay of diabetes and chronic kidney disease in the American Indian and Alaska Native population. The brochure covers the prevention of diabetes, treatment and monitoring strategies for people who already have diabetes, the symptoms of kidney damage, the impact of high blood pressure (hypertension) and the importance of treating it, and treatment options for kidney failure (dialysis and transplantation). One sidebar highlights the symptoms

of diabetes. Three biographical outlines are included in the brochure; each one tells the story of one Native American person who has chronic kidney disease and diabetes. The brochure concludes with a brief description of the work and publications of the National Kidney Foundation (NKF, www.kidney.org).

- **Preventing Diabetic Kidney Disease**

  Source: New York, NY: National Kidney Foundation, Inc. 1993. 4 p.

  Contact: Available from National Kidney Foundation. U.S. Materials Orders, 30 East 33rd Street, New York, NY 10016. (212) 889-2210. Fax (212) 689-9261. PRICE: $7.00 for 25 copies. Item number: 02-30.

  Summary: Diabetic kidney disease (diabetic nephropathy) is a decrease in kidney function that occurs in some people who have diabetes. The fact sheet answers common questions about diabetic nephropathy, focusing on prevention. Topics include the causes of diabetic nephropathy, risk factors, diagnosis, the typical time span between diagnosis of diabetes and the evolution of kidney disease (for both type 1 and type 2 diabetes), strategies for preventing or retarding the progression of kidney disease, the use of ACE inhibitors, the incidence and prevalence of kidney disease in the population of people with diabetes, and the types of treatments available if one's kidneys fail altogether. The risk factors for diabetic nephropathy include high blood pressure (hypertension), poor glucose (sugar) control, inherited tendency to kidney disease, ethnicity, and diet. Some studies suggest that a group of high blood pressure medications called ACE inhibitors may help to prevent or delay the progression of diabetic nephropathy. The fact sheet concludes with a brief description of the activities of the National Kidney Foundation. (AA-M).

- **Working with Kidney Disease**

  Source: New York, NY: National Kidney Foundation. 1999. 7 p.

  Contact: Available from National Kidney Foundation. 30 East 33rd Street, Suite 1100, New York, NY 10016. (800) 622-9010 or (212) 889-2210. Fax (212) 689-9261. E-mail: info@kidney.org. Website: www.kidney.org. PRICE: Single copy free; bulk copies available.

  Summary: For people with kidney disease, rehabilitation includes returning to a healthier physical state, having a more positive outlook, enjoying relationships with family and friends, and feeling useful. This brochure answers common questions about finding, keeping, or changing jobs for people with kidney disease. The brochure emphasizes the importance of building one's strength and endurance as part of rehabilitation efforts, including the role of diet, anti anemia therapy (erythropoietin), and exercise. Topics covered include coping with illness, going back to work after treatment is established, local resources to help patients locate employment, how to prepare for job hunting, what to tell potential employers about one's illness and treatment, laws to protect kidney patients against job discrimination, health insurance considerations, disability benefits, Social Security work incentive programs, and the psychosocial benefits of working. The brochure concludes that hard work and determination are needed to cope with the changes caused by illness, but the results are well worth the effort. The brochure concludes with a list of instructional materials available from the NKF and a brief description of the activities of the organization (including their website at www.kidney.org).

- **Limiting Fluid When You Have Kidney Disease**

  Source: San Bruno, CA: Krames Communications. 1997. [2 p.].

  Contact: Available from Krames Communications. Order Department, 1100 Grundy Lane, San Bruno, CA 94066-9821. (800) 333-3032. Fax (650) 244-4512. Website: www.krames.com. PRICE: $12.50 for a pad of 50. Item number 5551.

  Summary: Healthy kidneys balance the amount of fluid that enters and leaves the body. This fact sheet helps readers with kidney disease understand the reasons why fluids need to be limited when one has kidney disease. The fact sheet first lists the items that fall into the category of fluid: water for drinking and taking medications, ice cubes and ice chips, coffee and tea, sodas, milk, cream and liquid creamer, juices (fruit and vegetable), soups, popsicles, ice cream, sherbets, sorbets, and gelatin. The next section helps readers understand the different ways of measuring fluids; a chart lists the equivalents among units of measure. The fact sheet leaves blank space for the health care provider to individualize the information about the patient's limitations for fluid. The latter half of the fact sheet offers strategies for ways to control thirst and to stay on the fluid limitations. The fact sheet also includes space for special instructions. The fact sheet is illustrated with simple line drawings of patients and everyday foods and beverages.

- **About Chronic Kidney Disease: A Guide for Patients and Their Families**

  Source: New York, NY: National Kidney Foundation, Inc. 2002. 24 p.

  Contact: Available from National Kidney Foundation, Inc. Medical Department, 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Fax: (212) 689-9261. E-mail: info@kidney.org. Website: www.kidney.org. PRICE: Contact organization for print copies.

  Summary: In many cases, early detection and treatment of kidney disease can help to prevent more serious kidney disease and other complications. This booklet, written for patients with chronic kidney disease and for their families, familiarizes readers with the prevention, detection, and treatment of kidney disease. The information in the booklet is based on the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) Clinical Practice Guidelines for Chronic Kidney Disease (CKD). Written in a question and answer format, the booklet covers the anatomy and physiology of the kidneys, a definition of CKD, the causes of CKD, the symptoms of kidney disease, the risk factors for kidney disease, tests that may be done to diagnose or identify CKD, how to reduce one's chances of developing kidney disease, diagnostic tests that may be performed to help judge the level of newly-diagnosed CKD, classification stages of CKD, treatment options for each stage, treatments that can slow the progression of kidney disease, treatment options for kidney failure, and lifestyle changes and psychosocial factors that may accompany a diagnosis of CKD. The booklet includes a summary of the key points covered, a posttest to quiz one's knowledge about CKD, and a glossary of common laboratory values. The booklet concludes with a list of publications available through the National Kidney Foundation, as well as a brief description of the work of the Foundation (www.kidney.org). The brochure is illustrated with black and white photographs. 5 figures. 1 table.

- **Staying Fit with Kidney Disease**

  Source: New York, NY: National Kidney Foundation. 2001. 5 p.

Contact: National Kidney Foundation. 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Fax (212) 689-9261. E-mail: info@kidney.org. Website: www.kidney.org. PRICE: Full-text available online at no charge.

Summary: In the past, people thought that patients with kidney disease would not be able to join in vigorous activity. Current thinking supports the idea that patients who decide to follow an exercise program have an increase in strength and energy. This brochure from the National Kidney Foundation (NKF) focuses on strategies to stay fit with kidney disease. Prior to the availability of erythropoietin (EPO), people often felt tired and weak and had difficulty exercising because of anemia. Now anemia can be treated, and patients feel more like exercising and are able to do more activity and achieve better results. In addition to increased energy levels, other benefits from exercise can include improved physical function, better blood pressure control, improved muscle strength, lowered level of blood fats (cholesterol and triglycerides), better sleep, and better control of body weight. In addition, patients who exercise are less depressed and worry less, are more able to do things for themselves, and feel better about themselves. Patients are encouraged to consult with their health care providers before starting an exercise program. The brochure notes that patients should then look at four aspects of the exercise program: the type of exercise, the length of time spent exercising, how often the exercise will happen, and how hard the exercise should be. The brochure also reviews the symptoms of too much exercising and the times when patients should not exercise. The brochure concludes with a list of instructional materials available from the NKF and a brief description of the activities of the organization (including their website at www.kidney.org).

- **Microalbuminuria in Diabetic Kidney Disease**

  Source: New York, NY: National Kidney Foundation. 1996. 5 p.

  Contact: Available from National Kidney Foundation of Southern California. 5777 West Century Boulevard, Suite 1450, Los Angeles, CA 90045-7404. (310) 641-8152. Fax (310) 641-5246. Website: www.kidneysocal.org. PRICE: Single copy free; bulk copies available.

  Summary: Kidney disease is one of the most serious complications of diabetes. After years of diabetes, the filtering units of the kidney (glomeruli) get scarred so that they cannot filter the blood efficiently. Eventually, the kidneys may fail completely so that the patient needs dialysis or a kidney transplant. This fact sheet offers readers with information about microalbuminuria in diabetic kidney disease. The risk factors for getting kidney disease for people with diabetes include having a family member with diabetic kidney disease (diabetic nephropathy), high blood glucose levels (hyperglycemia), high blood pressure (hypertension), and cigarette smoking. Microalbuminuria (microscopic protein in the urine) means that the kidney has some damage and is starting to spill some albumin (a kind of protein) in the urine. Microalbuminuria is measured by a specific urine test; routine urinalysis does not detect microalbuminuria. The microalbuminuria does not itself cause any symptoms. The fact sheet recommends that all people with diabetes (type 1 and type 2) should be tested for microalbuminuria. Readers are encouraged to keep their blood glucose levels in as tight control as possible, to lower the risk of all diabetes complications, including diabetic kidney disease. The fact sheet concludes with a brief description of the National Kidney Foundation (NKF) and its activities.

- **Quick Reference Clinical Handbook for Chronic Kidney Disease**

  Source: New York, NY: National Kidney Foundation (NKF). 2001. 33 p.

Contact: Available from National Kidney Foundation (NKF). 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Website: www.kidney.org. PRICE: Single copy free.

Summary: Millions of Americans are at risk for developing renal (kidney) disease or are already experiencing some symptoms of kidney disease. In an effort to prevent development or to delay progression of chronic kidney disease (CKD), these populations must be identified and appropriate treatment initiated early to optimize patient outcomes. This booklet highlights guidelines from the KDOQI 2000 Update that offers clinical practice guidelines for hemodialysis adequacy, peritoneal dialysis, vascular access, and the treatment of anemia in chronic kidney disease. The guidelines are organized according to patient presentation rather than numerical sequence. For easy cross referencing, all guideline recommendations are highlighted in bold text and identified by KDOQI topic and number. This handbook helps health care providers apply the statements and recommendations from KDOQI in their work with kidney patients. Decisions to adopt specific guideline recommendations must be made by practitioners in light of available resources and circumstances presented by individual patients. Specific topics include early patient preparation regarding treatment options, protecting arm veins, the types of and timing for hemodialysis access, patient evaluation prior to access placement, the indications for the initiation of renal replacement therapy, evaluating anemia, assessing and monitoring iron status, administering iron, oral iron, intravenous iron, iron dextran dosing guidelines for pediatric patients, administering epoetin (erythropoietin), hyporesponsiveness to epoetin, and the role of red blood cell transfusions. One section discusses patient education. The booklet concludes with a selected bibliography. 1 figure. 5 tables.

- **Are You at Increased Risk for Chronic Kidney Disease?**

Source: New York, NY: National Kidney Foundation (NKF). 2002. 8 p.

Contact: Available from National Kidney Foundation (NKF). 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Website: www.kidney.org. PRICE: Single copy free; $25.00 for 100 copies.

Summary: More than 20 million Americans (one in nine adults) have chronic kidney disease, and most are not even aware of it. More than 20 million others are at increased risk for kidney disease. Early detection and treatment help to keep kidney disease from getting worse. This booklet helps readers learn whether they are at increased risk for chronic kidney disease and what to do if they are in that population. The booklet first reviews the physiology of the kidneys, then defines and describes chronic kidney disease. The booklet also covers risk factors (diabetes, high blood pressure or hypertension, a family history of chronic kidney disease, older age); why African Americans and other ethnic groups are at increased risk for chronic kidney disease; strategies for people at increased risk of kidney disease; the symptoms of chronic kidney disease; diagnostic and monitoring tests that may be utilized, including glomerular filtration rate (GFR), ultrasound or CT scan, and kidney biopsy; the stages of chronic kidney disease; strategies to prevent chronic kidney disease from getting worse; treatment options; what happens if kidney failure occurs; and the related problem of cardiovascular disease risk in patients at risk of kidney diseases. The brochure concludes with a brief description of the National Kidney Foundation (NKF) and its publications and programs; the contact information for the organization is also provided (www.kidney.org). 1 table.

- **Diabetes and Kidney Disease: A Guide for American Indians and Alaska Natives**

  Source: New York, NY: National Kidney Foundation (NKF). 2000. 11 p.

  Contact: Available from National Kidney Foundation (NKF). 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Website: www.kidney.org. PRICE: Single copy free; $25.00 for 100 copies.

  Summary: One out of five American Indians and Alaska Natives has diabetes, compared with one of 20 adults in the total United States population. This brochure helps American Indians and Alaska Natives understand the interplay between diabetes mellitus and kidney disease. As a result of their high rate of diabetes, these populations develop kidney failure three times more often than white people. The brochure stresses that the best way to fight diabetes is to prevent it; this is especially the case for type 2 diabetes, which usually occurs in adults over age 45. Type 2 diabetes can be prevented or delayed by following a meal plan that is high in fiber and low in fat and simple sugars, getting plenty of exercise, and keeping body weight at healthy levels. The brochure also offers strategies for readers who have already been diagnosed with diabetes. The brochure reminds readers of the signs and symptoms of kidney disease, including albumin (protein) in the urine, high blood pressure, swelling in the ankles and legs, and the need to urinate more often (particularly at night). The brochure explains how dialysis and kidney transplants can be used for patients in whom kidney disease has caused kidney failure. The brochure concludes with a list of booklets available through the National Kidney Foundation. The brochure features sidebars sharing the stories of individual American Indians and Alaska Natives in their lives with diabetes. 5 figures.

- **Polycystic Kidney Disease (PKD) Information**

  Source: Kansas City, MO: Polycystic Kidney Disease (PKD) Foundation. 200x. 4 p.

  Contact: Available from Polycystic Kidney Disease (PKD) Foundation. 4901 Main Street, Suite 200, Kansas City, Missouri 64112-2634. (800) 753-2873 or (816) 931-2600. Fax: (816) 931-8655. E-mail: pkdcure@pkdcure.org. Website: www.pkdcure.org.

  Summary: Polycystic kidney disease (PKD) has two hereditary forms: autosomal dominant (ADPKD), the most common of all life-threatening genetic diseases; and autosomal recessive (ARPKD), a relatively rare disease that often causes mortality in the first month of life. This brochure offers basic information on PKD and current research on PKD. Topics include the epidemiology of PKD, how the disease is diagnosed, common PKD symptoms, genetic research, and patient care management. The brochure concludes that although once viewed as a hopelessly incurable disorder, PKD has emerged as a prime target for study and treatment. The brochure briefly describes the goals and activities of the PKD Foundation, the only organization devoted to programs of research to determine the cause, improve clinical treatment, and discover a cure for PKD. The contact information for the PKD Foundation is provided (www.pkdcure.org). 1 figure.

- **Polycystic Kidney Disease: The Most Common Life-Threatening Genetic Disease**

  Source: Kansas City, MO: Polycystic Kidney Research Foundation. 200x. [7 p.].

  Contact: Available from KD Foundation. 4901 Main Street, Suite 200, Kansas City, MO 64112-2634. (800) 753-2873 or (816) 931-2600. Fax: (816) 931-8655. E-mail: pkdcure@pkrfoundation.org. Website: www.kumc.edu/pkrf/. PRICE: Single copy free.

Summary: Polycystic kidney disease (PKD) is a disease that comes in two hereditary forms: autosomal dominant (ADPKD), the most common of all life threatening genetic diseases, or autosomal recessive (ARPKD), a relatively rare disease that often causes significant mortality in the first month of life. This brochure describes PKD and the work of the PKD Foundation, formerly called the Polycystic Kidney Research Foundation, an organization devoted to improving clinical treatment and discovering a cure for PKD. With the presence of PKD, cysts develop in both kidneys. There may be just a few cysts or many, and the cysts may range in size from a pinhead to the size of a grapefruit. Cysts are sacs of fluid that cause the kidney to enlarge and can hinder its filtering ability. Cysts also squeeze on blood vessels, forcing the pressure to rise. Beyond high blood pressure, symptoms of PKD include fatigue, frequent urination, blood in the urine, headaches, kidney stones, or urinary tract infections. ADPKD is not limited to the kidneys; common complications can include abnormalities in the vascular and cardiac systems. There are three main clinical tests used to diagnose PKD: ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI). Current research demonstrates that a person with ADPKD may play a major role in controlling the disease with regular health care maintenance, a good diet, and regular exercise. The booklet describes many of the PKD Foundation's activities in research funding and advances, public awareness, and education. The booklet concludes with an invitation for readers to join the PKD Foundation and send a donation to support the work of this organization. 2 figures.

- **Amyloidosis and Kidney Disease**

  Source: Bethesda, MD: National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH). 2001. 4 p.

  Contact: Available from National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). 3 Information Way, Bethesda, MD 20892-3580. (800) 891-5390 or (301) 654-4415. Fax (301)634-0716. E-mail: nkudic@info.niddk.nih.gov. Website: www.niddk.nih.gov/health/kidney/nkudic.htm. PRICE: Full-text available online at no charge; single copy free; bulk orders available. Order number: KU-145.

  Summary: Proteins circulate throughout the body in the blood and are normally harmless. Occasionally, cells produce abnormal proteins that can settle in body tissue, forming deposits and causing disease called amyloidosis. This fact sheet describes amyloidosis and the two types related to kidney disease. In primary amyloidosis, abnormal protein production occurs as a first step and can lead to kidney disease. Dialysis related amyloidosis (DRA), on the other hand, is a result of kidney disease. The fact sheet discusses these two types, including the symptoms, diagnosis, and therapy for each. No effective treatment has been found to reverse the effects of primary amyloidosis. DRA is relatively common in patients who have been on dialysis for more than 5 years, especially among the elderly. Some of the complications of DRA can be treated surgically. Although there is no cure for DRA, a successful kidney transplant can stop the disease from progressing. The fact sheet concludes with a brief list of resource organizations for more information and a brief description of the National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC) and its contact information. 1 figure.

- **Kidney Disease and Rehabilitation: The Role of the Facility Administrator**

  Source: New York, NY: National Kidney Foundation. 1999. 3 p.

Contact: Available from National Kidney Foundation. 30 East 33rd Street, Suite 1100, New York, NY 10016. (800) 622-9010 or (212) 889-2210. Fax (212) 689-9261. E-mail: info@kidney.org. Website: www.kidney.org. PRICE: Single copy free; bulk copies available.

Summary: Rehabilitation can include many things besides returning to work, such as education, exercise, volunteering, and family and community activities. This brochure is one in a series developed to help the members of the renal (kidney) treatment team better understand all aspects of ESRD patient rehabilitation and increase their involvement in rehabilitation. This brochure, written to describe the role of the facility administrator, reminds readers that the commitment to rehabilitation will have a positive economic impact on the facility, with decreased hospitalizations and an improvement in the overall well being of the patients. The brochure outlines the information that should be provided to assist in the rehabilitation of dialysis and transplantation patients; liability issues relating to rehabilitation; the costs and benefits associated with providing extended hours for dialysis; and costs and savings associated with encouraging rehabilitation. To evaluate the economic impact of a facility's rehabilitation program, the following should be taken into account: average number of nursing interventions in each dialysis treatment, the number of no shows or lost treatments due to hospitalization, the dollars generated on a per patient basis every month, source of payment, and the mortality rate. The brochure stresses that education of patients, staff, and the community is essential to furthering patient rehabilitation. A list of publications from the National Kidney Foundation (NKF) is offered, with a brief description of the organization and its activities.

- **KEEP: Kidney Early Evaluation Program: An Early Detection and Early Intervention Program for People at Increased Risk of Kidney Disease**

  Source: New York, NY: National Kidney Foundation, Inc. 2002. 6 p.

  Contact: Available from National Kidney Foundation, Inc. Medical Department, 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Fax: (212) 689-9261. E-mail: info@kidney.org. Website: www.kidney.org. PRICE: Contact organization for print copies.

  Summary: The Kidney Early Evaluation Program (KEEP) is a free health screening program designed to identify individuals at increased risk for kidney failure. The parent organization, the National Kidney Foundation, is committed to slowing or eliminating the progress of serious kidney disease. Family members of today's patients may never become tomorrow's patients because KEEP identified their problem and led to an effective prevention and treatment plant. The KEEP screening is a one-day health screening designed to identify individuals who are at a greater risk for developing kidney disease, to inform them of their risk, and to encourage these individuals to seek further evaluation and followup from a physician. This brochure describes the KEEP screening, including the program objectives, the screening process and tests that are done during the KEEP screening, the followup component, the research and evaluation aspects of the KEEP program, and comments about the screening program. 2 figures.

- **Executive Summary: Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, Stratification**

  Source: New York, NY: National Kidney Foundation (NKF). 2001. 28 p.

  Contact: Available from National Kidney Foundation (NKF). 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Website: www.kidney.org. PRICE: Single copy free.

Summary: This booklet highlights guidelines from the KDOQI (Kidney Disease Outcomes Quality Initiative) 2000 Update that establishes clinical practice guidelines to help improve outcomes for all individuals with kidney disease, from earliest kidney damage through the various stages of progression to kidney failure, when renalreplacement therapy becomes necessary. This booklet describes the activities and goals of the KDOQI Work Group on chronic kidney disease, the classification of chronic kidney disease (including the population at increased risk of developing chronic kidney disease), terminology and classification issues, the prevalence of chronic kidney disease in the United States, the review of evidence (including generalizability, the GFR or glomerular filtration rate range, results, methodological quality, and strength of evidence), and the future development of clinical guidelines. Fifteen guidelines are offered that cover the stages of chronic kidney disease, evaluation and treatment, individuals at increased risk of chronic kidney disease, the estimation of GFR, the assessment of proteinuria (protein in the urine), additional markers of chronic kidney disease, the association of level of GFR with hypertension (high blood pressure), the association of level of GFR with anemia, the association of level of GFR with nutritional status, bone disease and disorders of calcium and phosphorus metabolism, neuropathy (nerve disease), the association of level of GFR with indices of functioning and well being, factors associated with loss of kidney function in chronic kidney disease, the association of chronic kidney disease with diabetic complications, and the association of chronic kidney disease with cardiovascular disease. 2 figures. 8 references.

- **Treating Kidney Disease: A Team Approach**

  Source: McGaw Park, IL: Baxter Health Corporation. 1994. 9 p.

  Contact: Available from Baxter Healthcare Corporation, Renal Division. 1620 Waukegan Road, McGaw Park, IL 60085-6730. (800) 284-4060 or (708) 473-6030. PRICE: Single copy free.

  Summary: This booklet provides primary care physicians with information about treatment options for patients with kidney disease and the role that they can play in the consulting renal team. Topics include the importance of early patient referral; Federal law and patient rights; kidney transplantation; hemodialysis; peritoneal dialysis; patient survival rates, including morbidity and mortality; cost considerations; and support groups and patient associations. 6 tables. 11 references.

- **Getting the Most From Your Treatment: What You Need to Know When You Have Chronic Kidney Disease**

  Source: New York, NY: National Kidney Foundation (NKF). 2001. 31 p.

  Contact: Available from National Kidney Foundation (NKF). 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Website: www.kidney.org. PRICE: Single copy free.

  Summary: This booklet reviews guidelines for patients living with chronic kidney (renal) disease. Based on published clinical practice guidelines, the booklet helps patients become active in their own care. The booklet outlines chronic kidney disease, describes risk factors and screening or diagnostic tests that may be done, and discusses diet therapy, how to prevent bone disease and heart (cardiovascular) problems, how the treatment for anemia helps patients maintain their overall health, the different options for the treatment of kidney failure, and how to know when to start treatment for kidney failure. Diet and medications can help patients control the buildup of wastes in their blood, but if their kidney disease continues to progress, they may eventually develop kidney failure and need a treatment like dialysis or a kidney transplant. Monitoring tests

include the glomerular filtration rate and serum creatinine (both measures of kidney function). Treatments for kidney failure include hemodialysis, peritoneal dialysis, and kidney transplantation; the booklet guides readers through the decisions that need to be addressed regarding appropriate treatment options. The booklet concludes with a list of resources for additional information (all from the National Kidney Foundation) and an appendix that helps readers understand their laboratory values (results of the monitoring tests).

- **Diabetes and Kidney Disease**

  Source: New York, NY: Juvenile Diabetes Foundation International. 199x. [4 p.].

  Contact: Available from Juvenile Diabetes Foundation International. 120 Wall Street, New York, NY 10005-4001. (800) 533-2873 or (212) 785-9500. Website: www.jdfcure.com. PRICE: Single copy free; bulk copies available.

  Summary: This brochure discusses the effects of diabetes on the kidneys. People with either type 1 or type 2 diabetes are at risk for developing kidney disease. Diabetic nephropathy occurs because diabetes causes a change in the kidneys, killing some cells and causing the remaining ones to work harder. This eventually damages the small blood vessels in the kidneys, thus interfering with the filtering process. Untreated kidney damage can become renal failure. Protein in the urine is an early sign of kidney damage, so doctors perform tests to assess renal function as part of regular examinations. After diabetic kidney disease is diagnosed, various measures are used to slow the progression to end-stage renal disease. They include controlling blood sugar, high blood pressure, and urinary tract infections; using angiotensin converting enzyme inhibitors; and maintaining a low-protein diet. Treatment options for failed kidneys include hemodialysis and peritoneal dialysis, continuous ambulatory peritoneal dialysis, and kidney transplantation.

- **Facts About Kidney Diseases and Their Treatment**

  Source: Rockville, MD: American Kidney Fund. 1999. 13 p.

  Contact: Available from American Kidney Fund. 6110 Executive Boulevard, Suite 1010, Rockville, MD 20852. (800) 638-8299 or (301) 881-3052. Fax (301) 881-0898. E-mail: helpline@akfinc.org. Website: www.akfinc.org. PRICE: $0.30 plus shipping and handling.

  Summary: This brochure from the American Kidney Fund (AKF) informs the public about the signs, symptoms, and methods of treatment for various kidney diseases. The brochure begins by reviewing the anatomy and physiology of the kidneys, whose primary job is to remove waste from the blood and eliminate it in the urine. The kidneys also keep the right amount of fluid in the body by making more urine when there is too much fluid. Kidney disease is actually a catch all term that includes diseases ranging from urinary tract infections, to kidney stones, to more serious disorders such as polycystic kidney disease and glomerulonephritis. Many kidney diseases can be effectively treated if diagnosed in the early stages. The brochure stresses that high blood pressure (hypertension) can cause kidney disease and must be monitored and treated. The brochure reviews the more common diseases of the kidneys, including kidney stones, pyelonephritis (inflammation of kidney tissue due to infection), nephrosis (a condition in which the kidneys remove too much protein from the blood), glomerulonephritis (inflammation of the thin walled capillaries where filtration takes place), polycystic kidney disease, and end stage renal disease (ESRD). The brochure details the treatments available for ESRD, including hemodialysis, peritoneal dialysis,

and transplantation. The brochure concludes with a summary of facts to remember about kidney diseases, reiterating the importance of controlling high blood pressure. The back cover of the brochure briefly notes the goals and activities of the American Kidney Fund. 4 figures.

- **What Do I Need to Know About Preventing the Complications of Chronic Kidney Disease?**

  Source: Rockville, MD: American Kidney Fund. 2002. 32 p.

  Contact: Available from American Kidney Fund (AKF). 6110 Executive Boulevard, Suite 1010, Rockville, MD 20852. (8000) 638-8299 or (301) 881-3052 Fax (301) 881-0898. E-mail: helpline@akfinc.org. Website: www.kidneyfund.org. PRICE: 1-10 copies free; additional copies available at cost.

  Summary: This brochure helps readers newly diagnosed with renal insufficiency or early chronic kidney disease (CKD) understand how to take care of themselves and prevent the complications common to CKD. The brochure introduces readers to kidney disease, then discusses treatment options, the role of diet in treatment and prevention, possible complications associated with kidney disease, and the different types of doctors kidney disease patients normally encounter. Specific topics include a description of the physiology and function of the kidneys, symptoms of kidney disease, glomerular filtration rate (GFR, a measure of kidney function), the role of blood pressure control, diabetes control (when applicable), corticosteroids or other special medications, the need to avoid certain medications, protein restriction, caloric intake, carbohydrates, fats, fluid restriction, sodium, potassium, phosphorus, anemia, measuring hemoglobin (red blood cells), hypertension, vitamins and minerals, acidosis, and osteodystrophy (bone disease). The booklet includes sample menus, numerous charts of information, a summary of the concepts presented, and a glossary of terms. A list of resource organizations is also included, for readers wishing to obtain additional information. A reader's response questionnaire postage-paid postcard is appended to the brochure. 3 figures.

- **Diabetes and Chronic Kidney Disease**

  Source: New York, NY: National Kidney Foundation. 2002. 7 p.

  Contact: Available from National Kidney Foundation, Inc. Medical Department, 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Fax: (212) 689-9261. E-mail: info@kidney.org. Website: www.kidney.org. PRICE: Full-text available online at no charge; contact organization for print copies.

  Summary: This brochure helps readers with chronic kidney disease and diabetes mellitus understand the impact of the two diseases together. Written primarily for readers with chronic kidney disease (CKD) who are then diagnosed with diabetes, the brochure covers the pathology of diabetes-induced kidney damage, how patients with diabetes can prevent kidney disease, the early and later signs of CKD in patients with diabetes, treatment options (ACE inhibitors, special diets, tighter control of diabetes), kidney failure in patients with diabetes, the use of kidney transplantation in patients with diabetes, kidney-pancreas transplants, and the use of hemodialysis or peritoneal dialysis. The brochure concludes with a summary of the points covered in the text, a list of other resources for additional information, and a brief description of the activities and goals of the National Kidney Foundation (NKF). Black-and-white photographs of people illustrate the brochure. 1 table.

- **Treating Anemia in Early Kidney Disease**

  Source: New York, NY: National Kidney Foundation. 1994. 4 p.

  Contact: Available from National Kidney Foundation. 30 East 33 Street, New York, NY 10016. (800) 622-9010. PRICE: Single copy free.

  Summary: This brochure provides general information about the anemia often associated with early kidney disease. Written in a question-and-answer format, the brochure covers topics including reduced kidney function; causes of kidney disease; how kidney disease is treated; why people with kidney disease get anemia; how anemia can be treated; erythropoietin (EPO); side effects of EPO treatment; how kidney disease can affect the bones; diet therapy and the role of protein restriction; and the importance of exercise and maintaining overall health. The brochure encourages readers to consult their health care providers for more information and includes blank space for readers to record any questions that they may have. The brochure concludes with a brief description of the National Kidney Foundation (NKF).

- **My Food Plan for Early Kidney Disease**

  Source: Minneapolis, MN: IDC Publishing. 2000. [4 p.].

  Contact: Available from International Diabetes Center. 3800 Park Nicollet Boulevard, Minneapolis, MN 55416-2699. (888) 825-6315. Website: www.idcdiabetes.org. PRICE: $1.30 plus shipping and handling. Order number 2058-MFPK.

  Summary: This brochure provides people who have diabetes and early kidney disease with self care advice for managing these conditions. A special food plan can help control the buildup of waste products in the body and reduce the workload for the kidneys. People who have kidney disease need to pay attention to the amount of sodium, protein, and phosphorous in their food. In addition, controlling blood glucose levels is important when a person has early kidney disease because high blood glucose levels can further damage the kidneys. The brochure includes lists of carbohydrate choices, vegetables, meat and meat substitutes, fats, and free foods. Other topics include ways to use food labels and to create healthy, low sodium meals. In addition, the brochure includes a page for recording a personal food plan.

- **Vitamins and Minerals in Kidney Disease**

  Source: New York, NY: National Kidney Foundation. 1998. 7 p.

  Contact: Available from National Kidney Foundation. 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Website: www.kidney.org. PRICE: Single copy free.

  Summary: This brochure summarizes the role of vitamins and minerals in kidney disease. Written in a question and answer format, the brochure helps patients on dialysis determine how to use vitamin and mineral supplements. Vitamins and minerals are defined as substances needed by the body to help carry out special functions. Healthy people who can eat foods from all the food groups eat a variety of meats, grains, fruits, vegetables, and dairy products. However, people on a renal diet are limited in some food groups and therefore may not be getting all of the vitamins and minerals needed each day. Kidney disease changes the need for some nutrients; the brochure lists the reasons for these changes. The brochure then briefly discusses the supplements commonly prescribed, including vitamin C, B complex vitamins, iron, and calcium (used as a phosphorus binder). One of the important functions of vitamin B6, B12, and folic acid (the B complex vitamins) is to work together with erythropoietin

(EPO) and iron to prevent anemia. The brochure also details the problems that can arise from taking too many vitamins or minerals. The brochure concludes by encouraging readers to talk about nutrition with their health care providers and to contact the National Kidney Foundation (NKF) for more information. The brochure is one in a series of materials from an educational program of the National Kidney Foundation Dialysis Outcomes Quality Initiative.

- **Your Child, Your Family and Autosomal Recessive Polycystic Kidney Disease. 2nd ed**

  Source: Kansas City, MO: Polycystic Kidney Research Foundation. 1996. 26 p.

  Contact: Available from Polycystic Kidney Research Foundation. 4901 Main Street, Suite 320, Kansas City, MO 64112-2674. (800) PKD-CURE or (816) 931-2600. Fax (816) 931-8655. World Wide Web: http://www.kumc.edu/pkrf/. PRICE: $10.00 (members); $15.00 (for nonmembers).

  Summary: This detailed booklet is designed to educate families about autosomal recessive polycystic kidney disease (ARPKD), which is sometimes referred to as infantile polycystic kidney disease. The booklet explains how the kidneys work; how ARPKD affects the kidneys and the liver; the genetics of ARPKD, which occurs in 1 to 2 of every 10,000 births; diagnosis and prenatal genetic testing; and the differences between ARPKD and other kinds of kidney disease. The authors discuss the major health problems in ARPKD, treatment, outlook, how to ensure appropriate medical care, family issues, and current research. 7 figures.

- **Polycystic Kidney Disease**

  Source: Bethesda, MD: National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). 1996. 6 p.

  Contact: Available from National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). 3 Information Way, Bethesda, MD 20892-3580. (800) 891-5390 or (301) 654-4415. Fax (301)634-0716. E-mail: nkudic@info.niddk.nih.gov. Website: http://www.niddk.nih.gov/health/kidney/nkudic.htm. PRICE: Full-text available online at no charge; single copy free; bulk orders available. Order number: KU-105.

  Summary: This fact sheet describes polycystic kidney disease (PKD), a genetic disorder characterized by the growth of numerous cysts in the kidneys. The fact sheet explains the differences between autosomal dominant PKD (ADPKD), autosomal recessive PKD (ARPKD), and acquired cystic kidney disease (ACKD). For each, the fact sheet notes the etiology, symptoms, diagnostic considerations, and treatment options. A final section describes present research into the genetic components of PKD. The fact sheet concludes with a brief description of the National Kidney and Urologic Diseases Information Clearinghouse. 1 table.

- **New Treatments Being Studied for Kidney Disease in Lupus**

  Source: New York, NY: National Kidney Foundation. 1999. 2 p.

  Contact: Available from National Kidney Foundation, Inc. Medical Department, 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Fax: (212) 689-9261. E-mail: info@kidney.org. Website: www.kidney.org. PRICE: Full-text available online at no charge.

  Summary: This fact sheet describes some new treatments that are currently being studied for kidney disease that accompanies lupus erythematosus. Lupus is a chronic

illness where the body's immune system becomes overactive and attacks normal tissue. About a third of lupus patients develop kidney disease that requires treatment. The severity of lupus kidney disease (lupus nephritis) varies from minor abnormalities to complete kidney failure requiring dialysis or a kidney transplant. The fact sheet reviews the symptoms of lupus nephritis, the diagnostic tests used to confirm the condition, the two major forms of drug therapy, and newer therapies for lupus nephritis (including studies of newer drugs that suppress the immune system). Readers are encouraged to contact the National Kidney Foundation for more information.

- **Protein and Progressive Kidney Disease**

  Source: South Deerfield, MA: Channing L. Bete Co., Inc. 2000. 2 p.

  Contact: Available from Channing L. Bete Co., Inc. 200 State Road, South Deerfield, MA 01373. (800) 628-7733. Fax (800) 499-6464. Website: www.channing-bete.com. PRICE: $14.90 each; 100 sheets per tear sheet pad; discounts available for larger quantities. Order number 97588A-12-99.

  Summary: This fact sheet explains how eating the right balance of foods is a key to slowing down progressive kidney disease and helping patients to stay healthy. The fact sheet reviews why getting the right amount of protein is important, the need to work closely with one's health care providers (including the dietitian), how to know how much protein is recommended, animal protein compared to non animal protein, and the information available on the Nutrition Facts label. Protein and other nutrients make wastes that end up in the blood. Kidneys that are not working properly do not remove these wastes adequately; these wastes can build up and make patients more ill. However, eating too little protein can also be harmful as the body needs protein for healthy muscles and healing. The amount of protein recommended varies by body weight and treatment (dialysis versus no dialysis, and the presence of a kidney transplant). Readers are encouraged to ask their health care team for more information about their individual needs for protein, other nutrients, calories, fluids and fiber, and vitamin and mineral supplements. A few blank lines are provided for readers to take notes on their own specific guidelines or the dietitian's instructions. 5 figures.

- **Kidney Disease of Diabetes**

  Source: Bethesda, MD: National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). 1995. 6 p.

  Contact: Available from National Diabetes Information Clearinghouse (NDIC). 1 Information Way, Bethesda, MD 20892-3560. (800) 860-8747 or (301) 654-3327. Fax (301) 634-0716. E-mail: ndic@info.niddk.nih.gov. Also available at http://www.niddk.nih.gov/. PRICE: Full-text available online at no charge; single copy free; bulk copies available.

  Summary: This fact sheet informs readers about end-stage renal (kidney) disease (ESRD) associated with diabetes. The fact sheet stresses that, even when drugs and diet are able to control diabetes, the disease can lead to nephropathy and ESRD. Topics include noninsulin-dependent diabetes (NIDDM); insulin-dependent diabetes (IDDM); the five stages in the progression to ESRD in people with diabetes; the effects of high blood pressure; steps to prevent and slow kidney disease, including blood pressure medicines, low-protein diets, and intensive diabetes management; dialysis and transplantation; and present research strategies in this area. The fact sheet concludes with a brief description

of the activities of the National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). 1 figure. 3 references.

- **Practical Suggestions for Parents of Children with Chronic Kidney Disease**

  Source: New York, NY: National Kidney Foundation, Inc. 1991. 3 p.

  Contact: Available from National Kidney Foundation, Inc. 30 East 33rd Street, New York, NY 10016. (301) 235-2526 or (800) 622-9010. PRICE: Single copy free.

  Summary: This fact sheet presents practical suggestions for parents of children newly-diagnosed with chronic kidney disease. Suggestions provided and discussed include: learning about the disease and its treatments, actively participating in the child's care, helping the child take control of the illness, helping the child understand and accept diet restrictions, not letting medicine ruin the day, sharing experiences with others, and contacting the local National Kidney Foundation affiliate for support and services.

- **Lupus and Kidney Disease**

  Source: New York, NY: National Kidney Foundation. 1992. 3 p.

  Contact: Available from National Kidney Foundation. 30 East 33rd Street, New York, NY 10016. (800) 622-9010. PRICE: Single copy free.

  Summary: This fact sheet provides basic information about lupus erythematosus and kidney disease. Written in a question and answer format, the fact sheet defines lupus and then covers its causes; symptoms; how lupus can harm the kidneys; diagnosis and treatment; side effects of immunosuppressive drugs used to treat lupus; dietary considerations; diagnosing any kidney problems related to lupus; what happens if the kidneys fail; the long-term prognosis for patients with lupus; and patient self-care and management considerations. The fact sheet concludes with a brief description of the National Kidney Foundation (NKF) and its activities.

- **Kidney Disease: Options for Prevention and Treatment**

  Source: Alexandria, VA: American Diabetes Association. 199x. 6 p.

  Contact: Available from American Diabetes Association, Inc. Order Fulfillment Department, P.O. Box 930850, Atlanta, GA 31193-0850. (800) 232-6733. Fax (770) 442-9742. PRICE: $9.95 (members), $11.95 (nonmembers) for 50 copies; single copy free. Order number CDBD36.

  Summary: This fact sheet, which is one in a series of 42 fact sheets about daily living and coping with diabetes, provides information on kidney disease in people with diabetes. Topics include how diabetes can damage kidneys, populations at risk for kidney disease, symptoms and diagnosis, prevention, kidney disease treatments, kidney transplants, dialysis, hemodialysis, peritoneal dialysis, and the financial costs of dialysis and kidney transplants. Factors that can influence the development of kidney disease include genetics, blood glucose control, and blood pressure. The fact sheet notes that most people who get diabetic kidney disease also have diabetic eye problems. (AA-M).

- **Slowing Progressive Kidney Disease Self Care Handbook**

  Source: South Deerfield, MA: Channing L. Bete Co., Inc. 2000. 31 p.

Contact: Available from Channing L. Bete Co., Inc. 200 State Road, South Deerfield, MA 01373. (800) 628-7733. Fax (800) 499-6464. Website: www.channing-bete.com. PRICE: $2.73 each for 1-99 copies; discounts available for larger quantities. Order number 97571.

Summary: This handbook provides people who have diabetes with information on slowing the progression of kidney disease. The kidneys clean blood, maintain healthy balances of fluids and nutrients, keep blood pressure at healthy levels, and keep bones healthy. Causes of kidney disease include diabetes, high blood pressure, inherited conditions, infection, medications, and use of alcohol or drugs. During the early stage of kidney disease, about one half of the nephrons have stopped working. In later stages, the number of nephrons that stop working keeps growing. By the time a person has reached end stage renal disease (ESRD), about nine in 10 nephrons have stopped working and a person needs dialysis or kidney transplantation to live. The handbook outlines the symptoms of kidney disease, describes some of the tests used to diagnose kidney disease, and identifies the functions of the members of a person's health care team. Another topic is the components of a treatment plan for kidney disease, including controlling other medical conditions, planning a proper diet, making other healthy changes, taking prescribed medications, and undergoing follow-up tests. In addition, the handbook discusses treatments for ESRD, including hemodialysis, continuous ambulatory peritoneal dialysis, continuous cycling peritoneal dialysis, and kidney transplantation. The handbook concludes by identifying sources of support and information.

- **Taking Charge of Your Health: A Guide for African Americans at Risk for Kidney Disease**

  Source: Cincinnati, OH: Kidney Foundation of Greater Cincinnati. 199x.

  Contact: Available from Kidney Foundation of Greater Cincinnati. 220 Victory Parkway, Suite 510, Cincinnati, OH 45206. (513) 961-8105. Fax (513) 961-8120. PRICE: Single copy free.

  Summary: This information packet provides a variety of health promotion materials, primarily on kidney disease, high blood pressure (hypertension), and organ donation, designed to educate African Americans about their particular health risks. The packet includes brochures on a medication aid program, urinary tract disorders (Scriptographic booklet, featuring simple cartoon drawings and nontechnical language), kidney dialysis and transplants (Scriptographic booklet), organ and tissue donation (Scriptographic booklet), treatment options for kidney failure, peritoneal dialysis (PD) catheter analysis, a general guide on kidney disease (from the American Kidney Fund, or AKF), facts about kidney stones, a guide for the dentist about the dialysis patient, central line access for hemodialysis, high blood pressure and kidney disease (a brochure specifically targeting African Americans), diabetes and kidney disease (also specifically targeting African Americans), and four brochures from the African American Health Education Program of the Kidney Foundation of Greater Cincinnati (covering the role of the kidneys, diabetes, high blood pressure, and the health program itself). The packet also includes fact sheets for people with kidney disease on getting the right amount of protein, limiting fluid, balancing calcium and phosphorus, and eating a safe amount of potassium. The materials are presented in a brightly colored folder, with basic information reiterated on the flaps of the folder.

- **Working With Kidney Disease: Rehabilitation and Employment**

  Source: New York, NY: National Kidney Foundation. 2001. 15 p.

Contact: National Kidney Foundation. 30 East 33rd Street, New York, NY 10016. (800) 622-9010. Fax (212) 689-9261. E-mail: info@kidney.org. Website: www.kidney.org. PRICE: Full-text available online at no charge.

Summary: This pamphlet emphasizes the importance that productive work and self-sufficiency can hold for people who have kidney disease. Potential problems and suggested solutions are outlined regarding rehabilitation and employment for those with kidney disease. Written in a question and answer format, the brochure discusses restoring physical and emotional strength; leaves of absence from work; community resources and preparation for job hunting; handling discussion of health issues in a job interview; job discrimination in light of the Americans with Disabilities Act (ADA); physical exams and company health insurance; grievance channels; and supplemental income.

- **Kidney Disease and Lupus**

  Source: Rockville, MD: Lupus Foundation of America. 1999. 6 p.

  Contact: Available from Lupus Foundation of America. 1300 Piccard Drive, Suite 200, Rockville, MD 20850-4303. (800) 558-0121 or (301) 670-9292. Fax (301) 670-9486. Website: www.lupus.org/lupus. PRICE: Available as part of a package of 21 different lupus related brochures for $3.95 plus shipping and handling.

  Summary: This pamphlet provides people who have systemic lupus erythematosus (SLE) with information on the kidney disease that accompanies it. This type of kidney disease, which is known as lupus nephritis or lupus glomerulonephritis, may affect about one third of those who have SLE. Symptoms that indicate the possibility of lupus nephritis include foamy, frothy urine; nocturnal urination; and fluid retention with weight gain and swelling. The clinical path of lupus nephritis is highly variable, with some people experiencing mild abnormalities and others experiencing more persistent, severe ones. Studies that can be performed to test for lupus nephritis are urinalysis, blood studies, 24 hour urine collection, imaging, and kidney biopsy. Corticosteroids and cytotoxic or immunosuppressive drugs are the major forms of drug therapy used to treat lupus nephritis. Despite treatment, some people may experience progressive loss of kidney function. These people will need hemodialysis or peritoneal dialysis and eventually kidney transplantation. The pamphlet also provides information on the Lupus Foundation of America. 1 table.

- **Introduction to Autosomal Dominant Polycystic Kidney Disease of The Adult-Onset Type**

  Source: Kansas City, MO: Polycystic Kidney Research (PKR) Foundation. 1995. 2 p.

  Contact: Available from Polycystic Kidney Research Foundation. 4901 Main Street, Suite 320, Kansas City, MO 64112-2674. (800) PKD-CURE. PRICE: Single copy free.

  Summary: This patient education fact sheet provides an introduction to autosomal dominant polycystic kidney disease (PKD) of the adult-onset type. Topics include the types of PKD; how PKD affects several internal organs; the role of the kidneys; kidney cysts and their formation; complications caused by the cysts; how a person gets PKD; testing for adult-type PKD; the prognosis for people with PKD; and lifestyle recommendations for PKD. The fact sheet is written in question and answer format, with answers provided in short, list style.

- **Anemia and Kidney Disease**

  Source: San Bruno, CA: Krames Communications. 1997. 2 p.

  Contact: Available from Krames Communications. 1100 Grundy Lane, San Bruno, CA 94066-3030. (800) 333-3032. Fax (415) 244-4512. PRICE: $12.50 for pad of 50 sheets.

  Summary: This patient education handout explains the basics of anemia and how it can become a problem for people with kidney disease. Anemia occurs when the blood does not have enough red cells; therefore, the blood cannot carry the necessary oxygen to the body. The handout lists the symptoms of anemia, including ongoing fatigue; shortness of breath; rapid, irregular heartbeat; trouble concentrating; erectile dysfunction (impotence); feeling dizzy or lightheaded; and constantly feeling cold. Normally, the kidneys send out a signal (erythropoietin) that tells the body when to make new red blood cells. But in people with kidney disease, the kidneys may not be able to send this signal. A medication called epoetin alfa (EPO), a synthetic version of erythropoietin, can be given. EPO controls anemia by signaling the body to make red blood cells. Most often, EPO is used to treat people on dialysis. The handout also discusses the role of iron in making blood cells. Most people who take EPO need extra iron. The handout offers a list of strategies for people who are taking iron (particularly suggestions for avoiding the constipation that can accompany iron intake). The handout is written in nontechnical language and is illustrated with colorful drawings.

- **Polycystic Kidney Disease (PKD)**

  Source: American Family Physician. 53(3): 935-936. February 15, 1996.

  Summary: This patient education handout provides information on polycystic kidney disease (PKD), an inherited disease in which cysts grow in the kidneys. Written in a question and answer format, the handout covers how PKD can affect one's daily life, PKD-related hypertension (high blood pressure), PKD and kidney failure, other organs that can be hurt by PKD, the symptoms of the disease, diagnostic considerations, PKD in infants, genetic considerations, diagnostic tests, and treatment options. The handout concludes with the names, addresses, and telephone numbers of two resource organizations: Polycystic Kidney Research Foundation and the National Kidney Foundation.

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search this site located at **http;//www.guideline.gov/** by using the keyword "kidney disease" (or synonyms). The following was recently posted:

- **Chronic kidney disease (non-dialysis) medical nutrition therapy protocol**

  Source: American Dietetic Association - Professional Association; 2002 May; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3293&nbr=2519&string=kidney+AND+disease

- **K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification**

  Source: National Kidney Foundation - Disease Specific Society; 2002 February; 246 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3192&nbr=2418&string=kidney+AND+disease

- **Management of chronic kidney disease and pre-ESRD in the primary care setting**

  Source: Department of Defense - Federal Government Agency [U.S.]; 2000 November; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3099&nbr=2325&string=kidney+AND+disease

- **NKF-K/DOQI clinical practice guidelines for anemia of chronic kidney disease: update 2000**

  Source: National Kidney Foundation - Disease Specific Society; 1997 (updated 2000); 67 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2784&nbr=2010&string=kidney+AND+disease

Healthfinder™

Healthfinder™ is sponsored by the U.S. Department of Health and Human Services and offers links to hundreds of other sites that contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines. The following was recently found in this database:

- **Amyloidosis and Kidney Disease**

  Summary: In recent years, researchers have discovered that different kinds of proteins can form amyloid deposits and have identified several types of amyloidosis.

  Source: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6489

- **An Introduction to the Kidneys and to PKD**

  Summary: To understand polycystic kidney disease, you must first understand how your kidneys operate as a primary organ within the makeup of the human body.

  Source: Polycystic Kidney Disease (PKD) Foundation

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7767

- **Anemia in Kidney Disease and Dialysis**

  Summary: Describes when anemia begins, its diagnosis, treatment, and causes other than kidney disease.

  Source: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6490

- **Growth Failure in Children with Kidney Disease**

  Summary: Describes the interactions among kidney disease, vitamins and minerals, and children's growth.

  Source: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6509

- **Kidney Disease of Diabetes**

  Summary: This consumer fact sheet discusses diabetes and end-stage renal disease (ESRD) and the treatments and therapies involved.

  Source: National Kidney and Urologic Diseases Information Clearinghouse, National Institute of Diabetes and Digestive and Kidney Disease

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=2085

- **National Kidney Disease Education Program**

  Summary: The National Kidney Disease Education Program aims to reduce morbidity and mortality from kidney disease by raising awareness about the seriousness of the problem and the importance of prevention,

  Source: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6705

- **Polycystic Kidney Disease**

  Summary: Polycystic kidney disease (PKD) is a genetic disorder characterized by the growth of numerous cysts in the kidneys. The cysts are filled with fluid.

  Source: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6525

- **RENALNET**

  Summary: RENALNET acts as a clearinghouse for information on the cause, treatment and management of kidney disease and End Stage Renal Disease(ESRD).

  Source: Nonprofit/Professional Entity--Follow the Resource URL for More Information

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=1359

- **Your Kidneys and How They Work**

  Summary: This resource explains what kidneys do, why and how they fail, the signs and detection of kidney disease, and treatment of kidney disease.

  Source: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6551

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 kidney disease. 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**

Associations and Kidney Disease

The following is a list of associations that provide information on and resources relating to kidney disease:

- **Autosomal Recessive Polycystic Kidney Disease Family Support**

  Telephone: (717) 529-6732

  Fax: (717) 529-6732

  Email: None.

  Web Site: None

  Background: Autosomal Recessive Polycystic **Kidney Disease** Family Support is a self-help organization dedicated to providing information and support to affected individuals and families, promoting professional and public awareness, and supporting research. Autosomal recessive polycystic **kidney disease** (ARPKD) is a rare inherited disorder that may be apparent at birth. Affected newborns often have poorly developed lungs, causing life-threatening complications in some cases. Infants with the disorder experience the development of multiple cysts in both kidneys, potentially causing severe enlargement of the kidneys. The progressive development of additional cysts and cyst enlargement may cause destruction of normal kidney tissue and associated kidney failure. Affected children may also experience abnormal widening of the liver's bile ducts, scarring around the ducts, and associated blockage of the liver's blood vessels (congenital hepatic fibrosis), which may cause enlargement of the liver and spleen, chronic bile duct infections, and eventual liver failure. In individuals with autosomal recessive polycystic **kidney disease,** the range and severity of associated symptoms and findings may vary greatly from case to case. Autosomal Recessive Polycystic **Kidney Disease** Family Support was established in 1993 and currently consists of approximately 100 members. The organization provides networking opportunities to affected families, conducts regular support group meetings with scheduled speakers, and offers a variety of educational materials including pamphlets and a regular newsletter. In addition, the organization is committed to promoting and supporting basic and clinical research and utilizing a database for research purposes.

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to kidney disease. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with kidney disease.

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 kidney disease. 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 "kidney disease" (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 "kidney disease". 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 "kidney disease" (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 "kidney disease" (or a synonym) into the search box, and click "Submit Query."

APPENDIX C. FINDING MEDICAL LIBRARIES

Overview

In this Appendix, we show you how to quickly find a medical library in your area.

Preparation

Your local public library and medical libraries have interlibrary loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[27]

Finding a Local Medical Library

The quickest method to locate medical libraries is to use the Internet-based directory published by the National Network of Libraries of Medicine (NN/LM). This network includes 4626 members and affiliates that provide many services to librarians, health professionals, and the public. To find a library in your area, simply visit **http://nnlm.gov/members/adv.html** or call 1-800-338-7657.

Medical Libraries in the U.S. and Canada

In addition to the NN/LM, the National Library of Medicine (NLM) lists a number of libraries with reference facilities that are open to the public. The following is the NLM's list and includes hyperlinks to each library's Web site. These Web pages can provide information on hours of operation and other restrictions. The list below is a small sample of

[27] Adapted from the NLM: **http://www.nlm.nih.gov/psd/cas/interlibrary.html**.

libraries recommended by the National Library of Medicine (sorted alphabetically by name of the U.S. state or Canadian province where the library is located)[28]:

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute)
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System, Humboldt), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos, **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**
- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** Los Gatos PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation, Sacramento), **http://suttermedicalcenter.org/library/**
- **California:** Health Sciences Libraries (University of California, Davis), **http://www.lib.ucdavis.edu/healthsci/**
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System, Pleasanton), **http://gaelnet.stmarys-ca.edu/other.libs/gbal/east/vchl.html**
- **California:** Washington Community Health Resource Library (Fremont), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.saintjosephdenver.org/yourhealth/libraries/**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**

[28] Abstracted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital, Waterbury), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute, Wilmington), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine, Wilmington), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia, Augusta), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia, Macon), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library, Honolulu), **http://hml.org/CHIS/**
- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center, Coeur d'Alene), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Chicago), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center, Peoria), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital, Lexington), **http://www.centralbap.com/education/community/library.cfm**
- **Kentucky:** University of Kentucky - Health Information Library (Chandler Medical Center, Lexington), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation, New Orleans), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital, Farmington), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center, Lewiston), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare, Bangor), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center, Portland), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital (Brunswick), **http://www.parkviewhospital.org/**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center, Biddeford), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital's Health Information Library (Western Maine Health, Norway), **http://www.wmhcc.org/Library/**

- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre, Winnipeg), **http://www.deerlodge.mb.ca/crane_library/about.asp**
- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital, Lowell), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital, Boston), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital, Southcoast Health System, New Bedford), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School, Worchester), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center, Ann Arbor), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information (Detroit), **http://www.henryford.com/body.cfm?id=39330**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center, Missoula)
- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**

- **Nevada:** Health Science Library, West Charleston Library (Las Vegas-Clark County Library District, Las Vegas), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library, Hanover), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital, Rahway), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center, Englewood), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center, Englewood), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York, Syracuse), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center, New Hyde Park), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** The Health Information Center at Saint Francis Hospital (Saint Francis Health System, Tulsa), **http://www.sfh-tulsa.com/services/healthinfo.asp**
- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center, The Dalles), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center, Hershey), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center, Danville), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital, Scranton), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System, Pittsburgh), **http://www.hsls.pitt.edu/guides/chi/hopwood/index_html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System, Williamsport), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System, Pittsburgh), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://www.mghlib.mcgill.ca/**

- **South Dakota:** Rapid City Regional Hospital Medical Library (Rapid City Regional Hospital), **http://www.rcrh.org/Services/Library/Default.asp**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center, Vancouver), **http://www.swmedicalcenter.com/body.cfm?id=72**

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://cancerweb.ncl.ac.uk/omd/**
- Rare Diseases Terms (Office of Rare Diseases): **http://ord.aspensys.com/asp/diseases/diseases.asp**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**

Beyond these, MEDLINEplus contains a very patient-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia can be accessed at **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as drkoop.com (**http://www.drkoop.com/**) and Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a**). The NIH suggests the following Web sites in the ADAM Medical Encyclopedia when searching for information on kidney disease:

- **Basic Guidelines for Kidney Disease**

  Kidney disease
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000457.htm

  Kidney disease - resources
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002172.htm

- **Background Topics for Kidney Disease**

  Kidney disease
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000457.htm

  Renal disorders
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001265.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**

KIDNEY DISEASE DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

5-Hydroxytryptophan: Precursor of serotonin used as antiepileptic and antidepressant. [NIH]

Abdomen: That portion of the body that lies between the thorax and the pelvis. [NIH]

Abdominal: Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Abdominal Pain: Sensation of discomfort, distress, or agony in the abdominal region. [NIH]

Aberrant: Wandering or deviating from the usual or normal course. [EU]

Ablate: In surgery, is to remove. [NIH]

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]

ACE: Angiotensin-coverting enzyme. A drug used to decrease pressure inside blood vessels. [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]

Acrylamide: A colorless, odorless, highly water soluble vinyl monomer formed from the hydration of acrylonitrile. It is primarily used in research laboratories for electrophoresis, chromatography, and electron microscopy and in the sewage and wastewater treatment industries. [NIH]

Acrylonitrile: A highly poisonous compound used widely in the manufacture of plastics, adhesives and synthetic rubber. [NIH]

Actin: Essential component of the cell skeleton. [NIH]

Action Potentials: The electric response of a nerve or muscle to its stimulation. [NIH]

Acute renal: A condition in which the kidneys suddenly stop working. In most cases, kidneys can recover from almost complete loss of function. [NIH]

Acute tubular: A severe form of acute renal failure that develops in people with severe illnesses like infections or with low blood pressure. Patients may need dialysis. Kidney function often improves if the underlying disease is successfully treated. [NIH]

Adaptability: Ability to develop some form of tolerance to conditions extremely different from those under which a living organism evolved. [NIH]

Adenocarcinoma: A malignant epithelial tumor with a glandular organization. [NIH]

Adenosine: A nucleoside that is composed of adenine and d-ribose. Adenosine or adenosine derivatives play many important biological roles in addition to being components of DNA and RNA. Adenosine itself is a neurotransmitter. [NIH]

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]

Adoptive Transfer: Form of passive immunization where previously sensitized immunologic agents (cells or serum) are transferred to non-immune recipients. When transfer of cells is used as a therapy for the treatment of neoplasms, it is called adoptive immunotherapy (immunotherapy, adoptive). [NIH]

Adrenal Cortex: The outer layer of the adrenal gland. It secretes mineralocorticoids, androgens, and glucocorticoids. [NIH]

Adrenal Glands: Paired glands situated in the retroperitoneal tissues at the superior pole of each kidney. [NIH]

Adrenergic: Activated by, characteristic of, or secreting epinephrine or substances with similar activity; the term is applied to those nerve fibres that liberate norepinephrine at a synapse when a nerve impulse passes, i.e., the sympathetic fibres. [EU]

Adverse Effect: An unwanted side effect of treatment. [NIH]

Aerobic: In biochemistry, reactions that need oxygen to happen or happen when oxygen is present. [NIH]

Affinity: 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

Agar: A complex sulfated polymer of galactose units, extracted from Gelidium cartilagineum, Gracilaria confervoides, and related red algae. It is used as a gel in the preparation of solid culture media for microorganisms, as a bulk laxative, in making emulsions, and as a supporting medium for immunodiffusion and immunoelectrophoresis. [NIH]

Age of Onset: The age or period of life at which a disease or the initial symptoms or manifestations of a disease appear in an individual. [NIH]

Agenesis: Lack of complete or normal development; congenital absence of an organ or part. [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]

Alanine: A non-essential amino acid that occurs in high levels in its free state in plasma. It is produced from pyruvate by transamination. It is involved in sugar and acid metabolism, increases immunity, and provides energy for muscle tissue, brain, and the central nervous system. [NIH]

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]

Albuminuria: More than normal amounts of a protein called albumin in the urine. Albuminuria may be a sign of kidney disease. [NIH]

Aldehydes: Organic compounds containing a carbonyl group in the form -CHO. [NIH]

Aldosterone: (11 beta)-11,21-Dihydroxy-3,20-dioxopregn-4-en-18-al. A hormone secreted by the adrenal cortex that functions in the regulation of electrolyte and water balance by increasing the renal retention of sodium and the excretion of potassium. [NIH]

Alertness: A state of readiness to detect and respond to certain specified small changes occurring at random intervals in the environment. [NIH]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [NIH]

Alimentary: Pertaining to food or nutritive material, or to the organs of digestion. [EU]

Alkaline: Having the reactions of an alkali. [EU]

Alkalosis: A pathological condition that removes acid or adds base to the body fluids. [NIH]

Alkylating Agents: Highly reactive chemicals that introduce alkyl radicals into biologically active molecules and thereby prevent their proper functioning. Many are used as antineoplastic agents, but most are very toxic, with carcinogenic, mutagenic, teratogenic, and immunosuppressant actions. They have also been used as components in poison gases. [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]

Allogeneic: Taken from different individuals of the same species. [NIH]

Allograft: An organ or tissue transplant between two humans. [NIH]

Allopurinol: A xanthine oxidase inhibitor that decreases uric acid production. [NIH]

Alopecia: Absence of hair from areas where it is normally present. [NIH]

Alprenolol: 1-((1-Methylethyl)amino)-3-(2-(2-propenyl)phenoxy)-2-propanol. Adrenergic beta-blocker used as an antihypertensive, anti-anginal, and anti-arrhythmic agent. [NIH]

Alternative medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used instead of standard treatments. Alternative medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Alveoli: Tiny air sacs at the end of the bronchioles in the lungs. [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]

Amikacin: A broad-spectrum antibiotic derived from kanamycin. It is reno- and ototoxic like the other aminoglycoside antibiotics. [NIH]

Amino Acid Sequence: The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

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]

Ammonia: A colorless alkaline gas. It is formed in the body during decomposition of organic materials during a large number of metabolically important reactions. [NIH]

Amplification: The production of additional copies of a chromosomal DNA sequence, found as either intrachromosomal or extrachromosomal DNA. [NIH]

Amyloid: A general term for a variety of different proteins that accumulate as extracellular fibrils of 7-10 nm and have common structural features, including a beta-pleated sheet conformation and the ability to bind such dyes as Congo red and thioflavine (Kandel, Schwartz, and Jessel, Principles of Neural Science, 3rd ed). [NIH]

Amyloidosis: A group of diseases in which protein is deposited in specific organs (localized amyloidosis) or throughout the body (systemic amyloidosis). Amyloidosis may be either primary (with no known cause) or secondary (caused by another disease, including some types of cancer). Generally, primary amyloidosis affects the nerves, skin, tongue, joints, heart, and liver; secondary amyloidosis often affects the spleen, kidneys, liver, and adrenal glands. [NIH]

Anabolic: Relating to, characterized by, or promoting anabolism. [EU]

Anaemia: A reduction below normal in the number of erythrocytes per cu. mm., in the quantity of haemoglobin, or in the volume of packed red cells per 100 ml. of blood which occurs when the equilibrium between blood loss (through bleeding or destruction) and blood production is disturbed. [EU]

Anaesthesia: Loss of feeling or sensation. Although the term is used for loss of tactile sensibility, or of any of the other senses, it is applied especially to loss of the sensation of pain, as it is induced to permit performance of surgery or other painful procedures. [EU]

Anal: Having to do with the anus, which is the posterior opening of the large bowel. [NIH]

Analgesic: An agent that alleviates pain without causing loss of consciousness. [EU]

Analog: In chemistry, a substance that is similar, but not identical, to another. [NIH]

Analogous: Resembling or similar in some respects, as in function or appearance, but not in origin or development;. [EU]

Analytes: A component of a test sample the presence of which has to be demonstrated. The term "analyte" includes where appropriate formed from the analyte during the analyses.

[NIH]

Anaphylatoxins: The family of peptides C3a, C4a, C5a, and C5a des-arginine produced in the serum during complement activation. They produce smooth muscle contraction, mast cell histamine release, affect platelet aggregation, and act as mediators of the local inflammatory process. The order of anaphylatoxin activity from strongest to weakest is C5a, C3a, C4a, and C5a des-arginine. The latter is the so-called "classical" anaphylatoxin but shows no spasmogenic activity though it contains some chemotactic ability. [NIH]

Anatomical: Pertaining to anatomy, or to the structure of the organism. [EU]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

Anemic: Hypoxia due to reduction of the oxygen-carrying capacity of the blood as a result of a decrease in the total hemoglobin or an alteration of the hemoglobin constituents. [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]

Angiopathy: Disease of the blood vessels (arteries, veins, and capillaries) that occurs when someone has diabetes for a long time. There are two types of angiopathy: macroangiopathy and microangiopathy. In macroangiopathy, fat and blood clots build up in the large blood vessels, stick to the vessel walls, and block the flow of blood. In microangiopathy, the walls of the smaller blood vessels become so thick and weak that they bleed, leak protein, and slow the flow of blood through the body. Then the cells, for example, the ones in the center of the eye, do not get enough blood and may be damaged. [NIH]

Angiotensin converting enzyme inhibitor: A drug used to decrease pressure inside blood vessels. [NIH]

Angiotensin-Converting Enzyme Inhibitors: A class of drugs whose main indications are the treatment of hypertension and heart failure. They exert their hemodynamic effect mainly by inhibiting the renin-angiotensin system. They also modulate sympathetic nervous system activity and increase prostaglandin synthesis. They cause mainly vasodilation and mild natriuresis without affecting heart rate and contractility. [NIH]

Angiotensinogen: An alpha-globulin of which a fragment of 14 amino acids is converted by renin to angiotensin I, the inactive precursor of angiotensin II. It is a member of the serpin superfamily. [NIH]

Animal model: An animal with a disease either the same as or like a disease in humans. Animal models are used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models. [NIH]

Anionic: Pertaining to or containing an anion. [EU]

Anions: Negatively charged atoms, radicals or groups of atoms which travel to the anode or positive pole during electrolysis. [NIH]

Anode: Electrode held at a positive potential with respect to a cathode. [NIH]

Anomalies: Birth defects; abnormalities. [NIH]

Anorexia: Lack or loss of appetite for food. Appetite is psychologic, dependent on memory and associations. Anorexia can be brought about by unattractive food, surroundings, or company. [NIH]

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]

Antiarrhythmic: An agent that prevents or alleviates cardiac arrhythmia. [EU]

Antibacterial: A substance that destroys bacteria or suppresses their growth or reproduction. [EU]

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

Antibodies: Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the antigen that induced their synthesis in cells of the lymphoid series (especially plasma cells), or with an antigen closely related to it. [NIH]

Antibody: A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. [NIH]

Anticoagulant: A drug that helps prevent blood clots from forming. Also called a blood thinner. [NIH]

Antidepressant: A drug used to treat depression. [NIH]

Antidiabetic: An agent that prevents or alleviates diabetes. [EU]

Antidote: A remedy for counteracting a poison. [EU]

Antiepileptic: An agent that combats epilepsy. [EU]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Antigen-Antibody Complex: The complex formed by the binding of antigen and antibody molecules. The deposition of large antigen-antibody complexes leading to tissue damage causes immune complex diseases. [NIH]

Antihypertensive: An agent that reduces high blood pressure. [EU]

Anti-infective: An agent that so acts. [EU]

Anti-inflammatory: Having to do with reducing inflammation. [NIH]

Anti-Inflammatory Agents: Substances that reduce or suppress inflammation. [NIH]

Antimetabolite: A chemical that is very similar to one required in a normal biochemical reaction in cells. Antimetabolites can stop or slow down the reaction. [NIH]

Antimitotic: Inhibiting or preventing mitosis. [EU]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

Antineoplastic Agents: Substances that inhibit or prevent the proliferation of neoplasms. [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]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Anuria: Inability to form or excrete urine. [NIH]

Anxiety: Persistent feeling of dread, apprehension, and impending disaster. [NIH]

Aorta: The main trunk of the systemic arteries. [NIH]

Aplastic anemia: A condition in which the bone marrow is unable to produce blood cells. [NIH]

Apnoea: Cessation of breathing. [EU]

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]

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]

Aromatic: Having a spicy odour. [EU]

Arrhythmia: Any variation from the normal rhythm or rate of the heart beat. [NIH]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arteriography: A procedure to x-ray arteries. The arteries can be seen because of an injection of a dye that outlines the vessels on an x-ray. [NIH]

Arteriolar: Pertaining to or resembling arterioles. [EU]

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Arteriovenous: Both arterial and venous; pertaining to or affecting an artery and a vein. [EU]

Arteriovenous Fistula: An abnormal communication between an artery and a vein. [NIH]

Arthrography: Roentgenography of a joint, usually after injection of either positive or negative contrast medium. [NIH]

Articular: Of or pertaining to a joint. [EU]

Aseptic: Free from infection or septic material; sterile. [EU]

Aspiration: The act of inhaling. [NIH]

Aspirin: A drug that reduces pain, fever, inflammation, and blood clotting. Aspirin belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is also being studied in cancer prevention. [NIH]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Astringents: Agents, usually topical, that cause the contraction of tissues for the control of bleeding or secretions. [NIH]

Astrocytes: The largest and most numerous neuroglial cells in the brain and spinal cord. Astrocytes (from "star" cells) are irregularly shaped with many long processes, including those with "end feet" which form the glial (limiting) membrane and directly and indirectly contribute to the blood brain barrier. They regulate the extracellular ionic and chemical environment, and "reactive astrocytes" (along with microglia) respond to injury. Astrocytes have high- affinity transmitter uptake systems, voltage-dependent and transmitter-gated ion channels, and can release transmitter, but their role in signaling (as in many other functions) is not well understood. [NIH]

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Ataxia: Impairment of the ability to perform smoothly coordinated voluntary movements. This condition may affect the limbs, trunk, eyes, pharnyx, larnyx, and other structures. Ataxia may result from impaired sensory or motor function. Sensory ataxia may result from posterior column injury or peripheral nerve diseases. Motor ataxia may be associated with cerebellar diseases; cerebral cortex diseases; thalamic diseases; basal ganglia diseases; injury to the red nucleus; and other conditions. [NIH]

Atrial: Pertaining to an atrium. [EU]

Atrial Fibrillation: Disorder of cardiac rhythm characterized by rapid, irregular atrial impulses and ineffective atrial contractions. [NIH]

Atrioventricular: Pertaining to an atrium of the heart and to a ventricle. [EU]

Atrium: A chamber; used in anatomical nomenclature to designate a chamber affording entrance to another structure or organ. Usually used alone to designate an atrium of the heart. [EU]

Atrophy: Decrease in the size of a cell, tissue, organ, or multiple organs, associated with a variety of pathological conditions such as abnormal cellular changes, ischemia, malnutrition, or hormonal changes. [NIH]

Attenuated: Strain with weakened or reduced virulence. [NIH]

Autoantibodies: Antibodies that react with self-antigens (autoantigens) of the organism that produced them. [NIH]

Autoantigens: Endogenous tissue constituents that have the ability to interact with autoantibodies and cause an immune response. [NIH]

Autodigestion: Autolysis; a condition found in disease of the stomach: the stomach wall is digested by the gastric juice. [NIH]

Autoimmune disease: A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. [NIH]

Autoimmunity: Process whereby the immune system reacts against the body's own tissues. Autoimmunity may produce or be caused by autoimmune diseases. [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]

Avian: A plasmodial infection in birds. [NIH]

Back Pain: Acute or chronic pain located in the posterior regions of the trunk, including the thoracic, lumbar, sacral, or adjacent regions. [NIH]

Backcross: A cross between a hybrid and either one of its parents. [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]

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]

Bacteriuria: The presence of bacteria in the urine with or without consequent urinary tract infection. Since bacteriuria is a clinical entity, the term does not preclude the use of urine/microbiology for technical discussions on the isolation and segregation of bacteria in the urine. [NIH]

Basal Ganglia: Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [NIH]

Basal Ganglia Diseases: Diseases of the basal ganglia including the putamen; globus pallidus; claustrum; amygdala; and caudate nucleus. Dyskinesias (most notably involuntary movements and alterations of the rate of movement) represent the primary clinical manifestations of these disorders. Common etiologies include cerebrovascular disease; neurodegenerative diseases; and craniocerebral trauma. [NIH]

Base: In chemistry, the nonacid part of a salt; a substance that combines with acids to form salts; a substance that dissociates to give hydroxide ions in aqueous solutions; a substance whose molecule or ion can combine with a proton (hydrogen ion); a substance capable of donating a pair of electrons (to an acid) for the formation of a coordinate covalent bond. [EU]

Base Pair Mismatch: The presence of an uncomplementary base in double-stranded DNA caused by spontaneous deamination of cytosine or adenine, mismatching during homologous recombination, or errors in DNA replication. Multiple, sequential base pair mismatches lead to formation of heteroduplex DNA (nucleic acid heteroduplexes). [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]

Baths: The immersion or washing of the body or any of its parts in water or other medium for cleansing or medical treatment. It includes bathing for personal hygiene as well as for medical purposes with the addition of therapeutic agents, such as alkalines, antiseptics, oil, etc. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body.

[NIH]

Benign tumor: A noncancerous growth that does not invade nearby tissue or spread to other parts of the body. [NIH]

Beta blocker: A drug used to slow the heart rate and reduce pressure inside blood vessels. It also can regulate heart rhythm. [NIH]

Beta-pleated: Particular three-dimensional pattern of amyloidoses. [NIH]

Bilateral: Affecting both the right and left side of body. [NIH]

Bile: An emulsifying agent produced in the liver and secreted into the duodenum. Its composition includes bile acids and salts, cholesterol, and electrolytes. It aids digestion of fats in the duodenum. [NIH]

Bile Acids: Acids made by the liver that work with bile to break down fats. [NIH]

Bile Acids and Salts: Steroid acids and salts. The primary bile acids are derived from cholesterol in the liver and usually conjugated with glycine or taurine. The secondary bile acids are further modified by bacteria in the intestine. They play an important role in the digestion and absorption of fat. They have also been used pharmacologically, especially in the treatment of gallstones. [NIH]

Bile Ducts: Tubes that carry bile from the liver to the gallbladder for storage and to the small intestine for use in digestion. [NIH]

Biliary: Having to do with the liver, bile ducts, and/or gallbladder. [NIH]

Biliary Tract: The gallbladder and its ducts. [NIH]

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]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

Biological response modifier: BRM. A substance that stimulates the body's response to infection and disease. [NIH]

Biological therapy: Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier (BRM) therapy. [NIH]

Biomarkers: Substances sometimes found in an increased amount in the blood, other body fluids, or tissues and that may suggest the presence of some types of cancer. Biomarkers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and GI tract cancers), and PSA (prostate cancer). Also called tumor markers. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

Biosynthesis: The building up of a chemical compound in the physiologic processes of a living organism. [EU]

Biotechnology: Body of knowledge related to the use of organisms, cells or cell-derived constituents for the purpose of developing products which are technically, scientifically and clinically useful. Alteration of biologic function at the molecular level (i.e., genetic engineering) is a central focus; laboratory methods used include transfection and cloning technologies, sequence and structure analysis algorithms, computer databases, and gene and protein structure function analysis and prediction. [NIH]

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]

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]

Body Fluids: Liquid components of living organisms. [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 Transplantation: The transference of bone marrow from one human or animal to another. [NIH]

Bone Remodeling: The continuous turnover of bone matrix and mineral that involves first, an increase in resorption (osteoclastic activity) and later, reactive bone formation (osteoblastic activity). The process of bone remodeling takes place in the adult skeleton at discrete foci. The process ensures the mechanical integrity of the skeleton throughout life and plays an important role in calcium homeostasis. An imbalance in the regulation of bone remodeling's two contrasting events, bone resorption and bone formation, results in many of the metabolic bone diseases, such as osteoporosis. [NIH]

Bone Resorption: Bone loss due to osteoclastic activity. [NIH]

Bowel: The long tube-shaped organ in the abdomen that completes the process of digestion. There is both a small and a large bowel. Also called the intestine. [NIH]

Bowel Movement: Body wastes passed through the rectum and anus. [NIH]

Bradykinin: A nonapeptide messenger that is enzymatically produced from kallidin in the blood where it is a potent but short-lived agent of arteriolar dilation and increased capillary permeability. Bradykinin is also released from mast cells during asthma attacks, from gut walls as a gastrointestinal vasodilator, from damaged tissues as a pain signal, and may be a

neurotransmitter. [NIH]

Branch: Most commonly used for branches of nerves, but applied also to other structures. [NIH]

Breakdown: A physical, metal, or nervous collapse. [NIH]

Breeding: The science or art of changing the constitution of a population of plants or animals through sexual reproduction. [NIH]

Broad-spectrum: Effective against a wide range of microorganisms; said of an antibiotic. [EU]

Bronchitis: Inflammation (swelling and reddening) of the bronchi. [NIH]

Buccal: Pertaining to or directed toward the cheek. In dental anatomy, used to refer to the buccal surface of a tooth. [EU]

Burns: Injuries to tissues caused by contact with heat, steam, chemicals (burns, chemical), electricity (burns, electric), or the like. [NIH]

Burns, Electric: Burns produced by contact with electric current or from a sudden discharge of electricity. [NIH]

Caffeine: A methylxanthine naturally occurring in some beverages and also used as a pharmacological agent. Caffeine's most notable pharmacological effect is as a central nervous system stimulant, increasing alertness and producing agitation. It also relaxes smooth muscle, stimulates cardiac muscle, stimulates diuresis, and appears to be useful in the treatment of some types of headache. Several cellular actions of caffeine have been observed, but it is not entirely clear how each contributes to its pharmacological profile. Among the most important are inhibition of cyclic nucleotide phosphodiesterases, antagonism of adenosine receptors, and modulation of intracellular calcium handling. [NIH]

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 Carbonate: Carbonic acid calcium salt (CaCO3). An odorless, tasteless powder or crystal that occurs in nature. It is used therapeutically as a phosphate buffer in hemodialysis patients and as a calcium supplement. [NIH]

Calcium channel blocker: A drug used to relax the blood vessel and heart muscle, causing pressure inside blood vessels to drop. It also can regulate heart rhythm. [NIH]

Calcium Channel Blockers: A class of drugs that act by selective inhibition of calcium influx through cell membranes or on the release and binding of calcium in intracellular pools. Since they are inducers of vascular and other smooth muscle relaxation, they are used in the drug therapy of hypertension and cerebrovascular spasms, as myocardial protective agents, and in the relaxation of uterine spasms. [NIH]

Calcium Channels: Voltage-dependent cell membrane glycoproteins selectively permeable to calcium ions. They are categorized as L-, T-, N-, P-, Q-, and R-types based on the activation and inactivation kinetics, ion specificity, and sensitivity to drugs and toxins. The L- and T-types are present throughout the cardiovascular and central nervous systems and the N-, P-, Q-, & R-types are located in neuronal tissue. [NIH]

Calcium Chloride: A salt used to replenish calcium levels, as an acid-producing diuretic, and as an antidote for magnesium poisoning. [NIH]

Calcium Hydroxide: Ca(OH)2. A white powder that has many therapeutic uses. Because of its ability to stimulate mineralization, it is found in many dental formulations. [NIH]

Calcium Signaling: Signal transduction mechanisms whereby calcium mobilization (from outside the cell or from intracellular storage pools) to the cytoplasm is triggered by external stimuli. Calcium signals are often seen to propagate as waves, oscillations, spikes or puffs. The calcium acts as an intracellular messenger by activating calcium-responsive proteins. [NIH]

Calculi: An abnormal concretion occurring mostly in the urinary and biliary tracts, usually composed of mineral salts. Also called stones. [NIH]

Callus: A callosity or hard, thick skin; the bone-like reparative substance that is formed round the edges and fragments of broken bone. [NIH]

Caloric intake: Refers to the number of calories (energy content) consumed. [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]

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]

Carcinogenic: Producing carcinoma. [EU]

Carcinogens: Substances that increase the risk of neoplasms in humans or animals. Both genotoxic chemicals, which affect DNA directly, and nongenotoxic chemicals, which induce neoplasms by other mechanism, are included. [NIH]

Carcinoma: Cancer that begins in the skin or in tissues that line or cover internal organs. [NIH]

Cardenolides: C(23)-steroids with methyl groups at C-10 and C-13 and a five-membered lactone at C-17. They are aglycone constituents of cardiac glycosides and must have at least one double bond in the molecule. the class includes cardadienolides and cardatrienolides. Members include digitoxin and digoxin and their derivatives and the strophanthins. [NIH]

Cardiac: Having to do with the heart. [NIH]

Cardiac Glycosides: Substances obtained from species of Digitalis, Strophanthus, and other plants that contain specific steroid glycosides or their semisynthetic derivatives and used in congestive heart failure. They increase the force of cardiac contraction without significantly affecting other parameters, but are very toxic at larger doses. Their mechanism of action usually involves inhibition of the Na(+)-K(+)-exchanging ATPase and they are often used in cell biological studies for that purpose. [NIH]

Cardiac Output: The volume of blood passing through the heart per unit of time. It is usually expressed as liters (volume) per minute so as not to be confused with stroke volume (volume per beat). [NIH]

Cardiotonic: 1. Having a tonic effect on the heart. 2. An agent that has a tonic effect on the heart. [EU]

Cardiotonic Agents: Agents that have a tonic effect on the heart or increase cardiac output. They may be glycosidic steroids related to Digitalis products, sympathomimetics, or other drugs and are used after myocardial infarcts, cardiac surgery, in shock, or in congestive heart failure. [NIH]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular disease: Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

Cardiovascular System: The heart and the blood vessels by which blood is pumped and circulated through the body. [NIH]

Carnitine: Constituent of striated muscle and liver. It is used therapeutically to stimulate gastric and pancreatic secretions and in the treatment of hyperlipoproteinemias. [NIH]

Carotene: The general name for a group of pigments found in green, yellow, and leafy vegetables, and yellow fruits. The pigments are fat-soluble, unsaturated aliphatic hydrocarbons functioning as provitamins and are converted to vitamin A through enzymatic processes in the intestinal wall. [NIH]

Carrier Proteins: Transport proteins that carry specific substances in the blood or across cell membranes. [NIH]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

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]

Caspase: Enzyme released by the cell at a crucial stage in apoptosis in order to shred all cellular proteins. [NIH]

Catecholamine: A group of chemical substances manufactured by the adrenal medulla and secreted during physiological stress. [NIH]

Catheters: A small, flexible tube that may be inserted into various parts of the body to inject or remove liquids. [NIH]

Cations: Postively charged atoms, radicals or groups of atoms which travel to the cathode or negative pole during electrolysis. [NIH]

Causal: Pertaining to a cause; directed against a cause. [EU]

Celecoxib: A drug that reduces pain. Celecoxib belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is being studied for cancer prevention. [NIH]

Celiac Disease: A disease characterized by intestinal malabsorption and precipitated by gluten-containing foods. The intestinal mucosa shows loss of villous structure. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell 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 Cycle: The complex series of phenomena, occurring between the end of one cell division and the end of the next, by which cellular material is divided between daughter cells. [NIH]

Cell Death: The termination of the cell's ability to carry out vital functions such as metabolism, growth, reproduction, responsiveness, and adaptability. [NIH]

Cell Differentiation: Progressive restriction of the developmental potential and increasing specialization of function which takes place during the development of the embryo and leads to the formation of specialized cells, tissues, and organs. [NIH]

Cell Division: The fission of a cell. [NIH]

Cell membrane: Cell membrane = plasma membrane. The structure enveloping a cell, enclosing the cytoplasm, and forming a selective permeability barrier; it consists of lipids, proteins, and some carbohydrates, the lipids thought to form a bilayer in which integral proteins are embedded to varying degrees. [EU]

Cell motility: The ability of a cell to move. [NIH]

Cell Polarity: Orientation of intracellular structures especially with respect to the apical and basolateral domains of the plasma membrane. Polarized cells must direct proteins from the Golgi apparatus to the appropriate domain since tight junctions prevent proteins from diffusing between the two domains. [NIH]

Cell proliferation: An increase in the number of cells as a result of cell growth and cell division. [NIH]

Cell Respiration: The metabolic process of all living cells (animal and plant) in which oxygen is used to provide a source of energy for the cell. [NIH]

Cell Survival: The span of viability of a cell characterized by the capacity to perform certain functions such as metabolism, growth, reproduction, some form of responsiveness, and adaptability. [NIH]

Central Nervous System: The main information-processing organs of the nervous system, consisting of the brain, spinal cord, and meninges. [NIH]

Centrifugation: A method of separating organelles or large molecules that relies upon differential sedimentation through a preformed density gradient under the influence of a gravitational field generated in a centrifuge. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

Cerebellum: Part of the metencephalon that lies in the posterior cranial fossa behind the brain stem. It is concerned with the coordination of movement. [NIH]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cerebral Angiography: Radiography of the vascular system of the brain after injection of a contrast medium. [NIH]

Cerebral Arteries: The arteries supplying the cerebral cortex. [NIH]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

Character: In current usage, approximately equivalent to personality. The sum of the relatively fixed personality traits and habitual modes of response of an individual. [NIH]

Chemokines: Class of pro-inflammatory cytokines that have the ability to attract and activate leukocytes. They can be divided into at least three structural branches: C (chemokines, C), CC (chemokines, CC), and CXC (chemokines, CXC), according to variations in a shared cysteine motif. [NIH]

Chemotactic Factors: Chemical substances that attract or repel cells or organisms. The concept denotes especially those factors released as a result of tissue injury, invasion, or immunologic activity, that attract leukocytes, macrophages, or other cells to the site of infection or insult. [NIH]

Chest Pain: Pressure, burning, or numbness in the chest. [NIH]

Child Behavior: Any observable response or action of a child from 24 months through 12 years of age. For neonates or children younger than 24 months, infant behavior is available. [NIH]

Chlorambucil: An anticancer drug that belongs to the family of drugs called alkylating agents. [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]

Chromatin: The material of chromosomes. It is a complex of DNA, histones, and nonhistone proteins (chromosomal proteins, non-histone) found within the nucleus of a cell. [NIH]

Chromosomal: Pertaining to chromosomes. [EU]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [NIH]

Chronic Disease: Disease or ailment of long duration. [NIH]

Chronic Obstructive Pulmonary Disease: Collective term for chronic bronchitis and emphysema. [NIH]

Chronic renal: Slow and progressive loss of kidney function over several years, often resulting in end-stage renal disease. People with end-stage renal disease need dialysis or transplantation to replace the work of the kidneys. [NIH]

Chylomicrons: A class of lipoproteins that carry dietary cholesterol and triglycerides from the small intestines to the tissues. [NIH]

Chymotrypsin: A serine endopeptidase secreted by the pancreas as its zymogen, chymotrypsinogen and carried in the pancreatic juice to the duodenum where it is activated by trypsin. It selectively cleaves aromatic amino acids on the carboxyl side. [NIH]

Ciliary: Inflammation or infection of the glands of the margins of the eyelids. [NIH]

Cilium: A hairlike appendage of the surface of a cell. It aids in cellular locomotion and creates currents in surrounding fluids. [NIH]

Clathrin: The main structural coat protein of coated vesicles which play a key role in the intracellular transport between membranous organelles. Clathrin also interacts with cytoskeletal proteins. [NIH]

Claudication: Limping or lameness. [EU]

Cleave: A double-stranded cut in DNA with a restriction endonuclease. [NIH]

Clinical Medicine: The study and practice of medicine by direct examination of the patient. [NIH]

Clinical trial: A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

Clone: The term "clone" has acquired a new meaning. It is applied specifically to the bits of inserted foreign DNA in the hybrid molecules of the population. Each inserted segment originally resided in the DNA of a complex genome amid millions of other DNA segment. [NIH]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Coated Vesicles: Vesicles formed when cell-membrane coated pits invaginate and pinch off. The outer surface of these vesicles are covered with a lattice-like network of coat proteins, such as clathrin, coat protein complex proteins, or caveolins. [NIH]

Codons: Any triplet of nucleotides (coding unit) in DNA or RNA (if RNA is the carrier of primary genetic information as in some viruses) that codes for particular amino acid or signals the beginning or end of the message. [NIH]

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]

Colitis: Inflammation of the colon. [NIH]

Collagen: A polypeptide substance comprising about one third of the total protein in mammalian organisms. It is the main constituent of skin, connective tissue, and the organic substance of bones and teeth. Different forms of collagen are produced in the body but all consist of three alpha-polypeptide chains arranged in a triple helix. Collagen is differentiated from other fibrous proteins, such as elastin, by the content of proline, hydroxyproline, and hydroxylysine; by the absence of tryptophan; and particularly by the high content of polar groups which are responsible for its swelling properties. [NIH]

Collapse: 1. A state of extreme prostration and depression, with failure of circulation. 2. Abnormal falling in of the walls of any part of organ. [EU]

Colloidal: Of the nature of a colloid. [EU]

Communis: Common tendon of the rectus group of muscles that surrounds the optic foramen and a portion of the superior orbital fissure, to the anterior margin of which it is attached at the spina recti lateralis. [NIH]

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]

Complementation: The production of a wild-type phenotype when two different mutations are combined in a diploid or a heterokaryon and tested in trans-configuration. [NIH]

Complete remission: The disappearance of all signs of cancer. Also called a complete response. [NIH]

Compress: A plug used to occludate an orifice in the control of bleeding, or to mop up secretions; an absorbent pad. [NIH]

Computational Biology: A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

Computed tomography: CT scan. A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized tomography and computerized axial tomography (CAT) scan. [NIH]

Computerized axial tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called CAT scan, computed tomography (CT scan), or computerized tomography. [NIH]

Computerized tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized axial tomography (CAT) scan and computed tomography (CT scan). [NIH]

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]

Conduction: The transfer of sound waves, heat, nervous impulses, or electricity. [EU]

Congestive heart failure: Weakness of the heart muscle that leads to a buildup of fluid in body tissues. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective

tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue Cells: A group of cells that includes fibroblasts, cartilage cells, adipocytes, smooth muscle cells, and bone cells. [NIH]

Consciousness: Sense of awareness of self and of the environment. [NIH]

Constipation: Infrequent or difficult evacuation of feces. [NIH]

Constriction: The act of constricting. [NIH]

Consultation: A deliberation between two or more physicians concerning the diagnosis and the proper method of treatment in a case. [NIH]

Consumption: Pulmonary tuberculosis. [NIH]

Continuum: An area over which the vegetation or animal population is of constantly changing composition so that homogeneous, separate communities cannot be distinguished. [NIH]

Contraceptive: An agent that diminishes the likelihood of or prevents conception. [EU]

Contractility: Capacity for becoming short in response to a suitable stimulus. [EU]

Contraindications: Any factor or sign that it is unwise to pursue a certain kind of action or treatment, e. g. giving a general anesthetic to a person with pneumonia. [NIH]

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]

Convulsions: A general term referring to sudden and often violent motor activity of cerebral or brainstem origin. Convulsions may also occur in the absence of an electrical cerebral discharge (e.g., in response to hypotension). [NIH]

Coordination: Muscular or motor regulation or the harmonious cooperation of muscles or groups of muscles, in a complex action or series of actions. [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 Artery Bypass: Surgical therapy of ischemic coronary artery disease achieved by grafting a section of saphenous vein, internal mammary artery, or other substitute between the aorta and the obstructed coronary artery distal to the obstructive lesion. [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]

Corpuscle: A small mass or body; a sensory nerve end bulb; a cell, especially that of the blood or the lymph. [NIH]

Cortex: The outer layer of an organ or other body structure, as distinguished from the internal substance. [EU]

Cortical: Pertaining to or of the nature of a cortex or bark. [EU]

Cortical Blindness: The inability to understand or interpret what is seen due to a disturbance in the cerebral associational areas, the retina, the sensory pathways, and the striate area being intact. [NIH]

Corticosteroid: Any of the steroids elaborated by the adrenal cortex (excluding the sex hormones of adrenal origin) in response to the release of corticotrophin (adrenocorticotropic hormone) by the pituitary gland, to any of the synthetic equivalents of these steroids, or to angiotensin II. They are divided, according to their predominant biological activity, into three major groups: glucocorticoids, chiefly influencing carbohydrate, fat, and protein metabolism; mineralocorticoids, affecting the regulation of electrolyte and water balance; and C19 androgens. Some corticosteroids exhibit both types of activity in varying degrees, and others exert only one type of effect. The corticosteroids are used clinically for hormonal replacement therapy, for suppression of ACTH secretion by the anterior pituitary, as antineoplastic, antiallergic, and anti-inflammatory agents, and to suppress the immune response. Called also adrenocortical hormone and corticoid. [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]

Cranial: Pertaining to the cranium, or to the anterior (in animals) or superior (in humans) end of the body. [EU]

Craniocerebral Trauma: Traumatic injuries involving the cranium and intracranial structures (i.e., brain; cranial nerves; meninges; and other structures). Injuries may be classified by whether or not the skull is penetrated (i.e., penetrating vs. nonpenetrating) or whether there is an associated hemorrhage. [NIH]

Creatinine: A compound that is excreted from the body in urine. Creatinine levels are measured to monitor kidney function. [NIH]

Crossing-over: The exchange of corresponding segments between chromatids of homologous chromosomes during meiosia, forming a chiasma. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Cutaneous: Having to do with the skin. [NIH]

Cyclic: Pertaining to or occurring in a cycle or cycles; the term is applied to chemical compounds that contain a ring of atoms in the nucleus. [EU]

Cyclophosphamide: Precursor of an alkylating nitrogen mustard antineoplastic and immunosuppressive agent that must be activated in the liver to form the active aldophosphamide. It is used in the treatment of lymphomas, leukemias, etc. Its side effect, alopecia, has been made use of in defleecing sheep. Cyclophosphamide may also cause sterility, birth defects, mutations, and cancer. [NIH]

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]

Cyst: A sac or capsule filled with fluid. [NIH]

Cysteine: A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

Cystine: A covalently linked dimeric nonessential amino acid formed by the oxidation of

cysteine. Two molecules of cysteine are joined together by a disulfide bridge to form cystine. [NIH]

Cystoscopy: Endoscopic examination, therapy or surgery of the urinary bladder. [NIH]

Cytogenetics: A branch of genetics which deals with the cytological and molecular behavior of genes and chromosomes during cell division. [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]

Cytoskeleton: The network of filaments, tubules, and interconnecting filamentous bridges which give shape, structure, and organization to the cytoplasm. [NIH]

Cytotoxic: Cell-killing. [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]

Data Collection: Systematic gathering of data for a particular purpose from various sources, including questionnaires, interviews, observation, existing records, and electronic devices. The process is usually preliminary to statistical analysis of the data. [NIH]

Databases, Bibliographic: Extensive collections, reputedly complete, of references and citations to books, articles, publications, etc., generally on a single subject or specialized subject area. Databases can operate through automated files, libraries, or computer disks. The concept should be differentiated from factual databases which is used for collections of data and facts apart from bibliographic references to them. [NIH]

Deamination: The removal of an amino group (NH2) from a chemical compound. [NIH]

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]

Decortication: Removal of part or all of the external surface of an organ. [NIH]

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]

Delivery of Health Care: The concept concerned with all aspects of providing and distributing health services to a patient population. [NIH]

Delusions: A false belief regarding the self or persons or objects outside the self that persists despite the facts, and is not considered tenable by one's associates. [NIH]

Dementia: An acquired organic mental disorder with loss of intellectual abilities of sufficient severity to interfere with social or occupational functioning. The dysfunction is multifaceted and involves memory, behavior, personality, judgment, attention, spatial relations, language, abstract thought, and other executive functions. The intellectual decline is usually progressive, and initially spares the level of consciousness. [NIH]

Denaturation: Rupture of the hydrogen bonds by heating a DNA solution and then cooling it rapidly causes the two complementary strands to separate. [NIH]

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

Depolarization: The process or act of neutralizing polarity. In neurophysiology, the reversal of the resting potential in excitable cell membranes when stimulated, i.e., the tendency of the cell membrane potential to become positive with respect to the potential outside the cell. [EU]

Depressive Disorder: An affective disorder manifested by either a dysphoric mood or loss of interest or pleasure in usual activities. The mood disturbance is prominent and relatively persistent. [NIH]

Deprivation: Loss or absence of parts, organs, powers, or things that are needed. [EU]

Dermal: Pertaining to or coming from the skin. [NIH]

Deuterium: Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [NIH]

Dexamethasone: (11 beta,16 alpha)-9-Fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione. An anti-inflammatory glucocorticoid used either in the free alcohol or esterified form in treatment of conditions that respond generally to cortisone. [NIH]

Diabetes Insipidus: A metabolic disorder due to disorders in the production or release of vasopressin. It is characterized by the chronic excretion of large amounts of low specific gravity urine and great thirst. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

Diabetic Retinopathy: Retinopathy associated with diabetes mellitus, which may be of the background type, progressively characterized by microaneurysms, interretinal punctuate macular edema, or of the proliferative type, characterized by neovascularization of the retina and optic disk, which may project into the vitreous, proliferation of fibrous tissue, vitreous hemorrhage, and retinal detachment. [NIH]

Diagnostic procedure: A method used to identify a disease. [NIH]

Dialyzer: A part of the hemodialysis machine. (See hemodialysis under dialysis.) The dialyzer has two sections separated by a membrane. One section holds dialysate. The other holds the patient's blood. [NIH]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diarrhoea: Abnormal frequency and liquidity of faecal discharges. [EU]

Diastole: Period of relaxation of the heart, especially the ventricles. [NIH]

Diastolic: Of or pertaining to the diastole. [EU]

Diastolic pressure: The lowest pressure to which blood pressure falls between contractions of the ventricles. [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 system: The organs that take in food and turn it into products that the body can use to stay healthy. Waste products the body cannot use leave the body through bowel movements. The digestive system includes the salivary glands, mouth, esophagus, stomach,

liver, pancreas, gallbladder, small and large intestines, and rectum. [NIH]

Digestive tract: The organs through which food passes when food is eaten. These organs are the mouth, esophagus, stomach, small and large intestines, and rectum. [NIH]

Digitalis: A genus of toxic herbaceous Eurasian plants of the Scrophulaceae which yield cardiotonic glycosides. The most useful are Digitalis lanata and D. purpurea. [NIH]

Dihydroxy: AMPA/Kainate antagonist. [NIH]

Dilatation: The act of dilating. [NIH]

Dilatation, Pathologic: The condition of an anatomical structure's being dilated beyond normal dimensions. [NIH]

Dilation: A process by which the pupil is temporarily enlarged with special eye drops (mydriatic); allows the eye care specialist to better view the inside of the eye. [NIH]

Dilazep: Coronary vasodilator with some antiarrhythmic activity. [NIH]

Diphenylamine: In humans it may be irritating to mucous membranes. Methemoglobinemia has been produced experimentally. In veterinary use, it is one of active ingredients in topical agents for prevention and treatment of screwworm infestation. An indicator in tests for nitrate poisoning. [NIH]

Diploid: Having two sets of chromosomes. [NIH]

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

Discrimination: The act of qualitative and/or quantitative differentiation between two or more stimuli. [NIH]

Disease Progression: The worsening of a disease over time. This concept is most often used for chronic and incurable diseases where the stage of the disease is an important determinant of therapy and prognosis. [NIH]

Disparity: Failure of the two retinal images of an object to fall on corresponding retinal points. [NIH]

Disposition: A tendency either physical or mental toward certain diseases. [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]

Disulphides: A covalent bridge formed by the oxidation of two cysteine residues to a cystine residue. The-S-S-bond is very strong and its presence confers additional stability. [NIH]

Dithiothreitol: A reagent commonly used in biochemical studies as a protective agent to prevent the oxidation of SH (thiol) groups and for reducing disulphides to dithiols. [NIH]

Diuresis: Increased excretion of urine. [EU]

Diuretic: A drug that increases the production of urine. [NIH]

Diverticula: Plural form of diverticulum. [NIH]

Diverticulitis: Inflammation of a diverticulum or diverticula. [NIH]

Diverticulum: A pathological condition manifested as a pouch or sac opening from a tubular or sacular organ. [NIH]

Dopamine: An endogenous catecholamine and prominent neurotransmitter in several systems of the brain. In the synthesis of catecholamines from tyrosine, it is the immediate precursor to norepinephrine and epinephrine. Dopamine is a major transmitter in the extrapyramidal system of the brain, and important in regulating movement. A family of dopaminergic receptor subtypes mediate its action. Dopamine is used pharmacologically for its direct (beta adrenergic agonist) and indirect (adrenergic releasing) sympathomimetic effects including its actions as an inotropic agent and as a renal vasodilator. [NIH]

Dose-dependent: Refers to the effects of treatment with a drug. If the effects change when the dose of the drug is changed, the effects are said to be dose dependent. [NIH]

Double-blinded: A clinical trial in which neither the medical staff nor the person knows which of several possible therapies the person is receiving. [NIH]

Drive: A state of internal activity of an organism that is a necessary condition before a given stimulus will elicit a class of responses; e.g., a certain level of hunger (drive) must be present before food will elicit an eating response. [NIH]

Drug Interactions: The action of a drug that may affect the activity, metabolism, or toxicity of another drug. [NIH]

Drug Tolerance: Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

Drug Toxicity: Manifestations of the adverse effects of drugs administered therapeutically or in the course of diagnostic techniques. It does not include accidental or intentional poisoning for which specific headings are available. [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]

Dysgenesis: Defective development. [EU]

Dyslipidemia: Disorders in the lipoprotein metabolism; classified as hypercholesterolemia, hypertriglyceridemia, combined hyperlipidemia, and low levels of high-density lipoprotein (HDL) cholesterol. All of the dyslipidemias can be primary or secondary. Both elevated levels of low-density lipoprotein (LDL) cholesterol and low levels of HDL cholesterol predispose to premature atherosclerosis. [NIH]

Dysmenorrhea: Painful menstruation. [NIH]

Dyspepsia: Impaired digestion, especially after eating. [NIH]

Dysplasia: Cells that look abnormal under a microscope but are not cancer. [NIH]

Dystrophy: Any disorder arising from defective or faulty nutrition, especially the muscular dystrophies. [EU]

Eclampsia: Onset of convulsions or coma in a previously diagnosed pre-eclamptic patient. [NIH]

Ectopic: Pertaining to or characterized by ectopia. [EU]

Edema: Excessive amount of watery fluid accumulated in the intercellular spaces, most commonly present in subcutaneous tissue. [NIH]

Effector: It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

Efficacy: The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomized control trial. [NIH]

Elastin: The protein that gives flexibility to tissues. [NIH]

Elective: Subject to the choice or decision of the patient or physician; applied to procedures that are advantageous to the patient but not urgent. [EU]

Electrocardiogram: Measurement of electrical activity during heartbeats. [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]

Emboli: Bit of foreign matter which enters the blood stream at one point and is carried until it is lodged or impacted in an artery and obstructs it. It may be a blood clot, an air bubble, fat or other tissue, or clumps of bacteria. [NIH]

Embolus: Bit of foreign matter which enters the blood stream at one point and is carried until it is lodged or impacted in an artery and obstructs it. It may be a blood clot, an air bubble, fat or other tissue, or clumps of bacteria. [NIH]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

Embryogenesis: The process of embryo or embryoid formation, whether by sexual (zygotic) or asexual means. In asexual embryogenesis embryoids arise directly from the explant or on intermediary callus tissue. In some cases they arise from individual cells (somatic cell embryoge). [NIH]

Emphysema: A pathological accumulation of air in tissues or organs. [NIH]

Enalapril: An angiotensin-converting enzyme inhibitor that is used to treat hypertension. [NIH]

Encephalocele: Cerebral tissue herniation through a congenital or acquired defect in the skull. The majority of congenital encephaloceles occur in the occipital or frontal regions. Clinical features include a protuberant mass that may be pulsatile. The quantity and location of protruding neural tissue determines the type and degree of neurologic deficit. Visual defects, psychomotor developmental delay, and persistent motor deficits frequently occur. [NIH]

Endemic: Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

Endocytosis: Cellular uptake of extracellular materials within membrane-limited vacuoles or microvesicles. Endosomes play a central role in endocytosis. [NIH]

Endopeptidases: A subclass of peptide hydrolases. They are classified primarily by their catalytic mechanism. Specificity is used only for identification of individual enzymes. They comprise the serine endopeptidases, EC 3.4.21; cysteine endopeptidases, EC 3.4.22; aspartic endopeptidases, EC 3.4.23, metalloendopeptidases, EC 3.4.24; and a group of enzymes yet to be assigned to any of the above sub-classes, EC 3.4.99. EC 3.4.-. [NIH]

Endosomes: Cytoplasmic vesicles formed when coated vesicles shed their clathrin coat. Endosomes internalize macromolecules bound by receptors on the cell surface. [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]

Enteropeptidase: A specialized proteolytic enzyme secreted by intestinal cells. It converts trypsinogen into its active form trypsin by removing the N-terminal peptide. EC 3.4.21.9. [NIH]

Environmental Exposure: The exposure to potentially harmful chemical, physical, or biological agents in the environment or to environmental factors that may include ionizing radiation, pathogenic organisms, or toxic chemicals. [NIH]

Environmental Health: The science of controlling or modifying those conditions, influences, or forces surrounding man which relate to promoting, establishing, and maintaining health. [NIH]

Enzymatic: Phase where enzyme cuts the precursor protein. [NIH]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

Eosinophils: Granular leukocytes with a nucleus that usually has two lobes connected by a slender thread of chromatin, and cytoplasm containing coarse, round granules that are

uniform in size and stainable by eosin. [NIH]

Epidemic: Occurring suddenly in numbers clearly in excess of normal expectancy; said especially of infectious diseases but applied also to any disease, injury, or other health-related event occurring in such outbreaks. [EU]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epidermal: Pertaining to or resembling epidermis. Called also epidermic or epidermoid. [EU]

Epidermal Growth Factor: A 6 kD polypeptide growth factor initially discovered in mouse submaxillary glands. Human epidermal growth factor was originally isolated from urine based on its ability to inhibit gastric secretion and called urogastrone. epidermal growth factor exerts a wide variety of biological effects including the promotion of proliferation and differentiation of mesenchymal and epithelial cells. [NIH]

Epidermis: Nonvascular layer of the skin. It is made up, from within outward, of five layers: 1) basal layer (stratum basale epidermidis); 2) spinous layer (stratum spinosum epidermidis); 3) granular layer (stratum granulosum epidermidis); 4) clear layer (stratum lucidum epidermidis); and 5) horny layer (stratum corneum epidermidis). [NIH]

Epigastric: Having to do with the upper middle area of the abdomen. [NIH]

Epinephrine: The active sympathomimetic hormone from the adrenal medulla in most species. It stimulates both the alpha- and beta- adrenergic systems, causes systemic vasoconstriction and gastrointestinal relaxation, stimulates the heart, and dilates bronchi and cerebral vessels. It is used in asthma and cardiac failure and to delay absorption of local anesthetics. [NIH]

Epithelial: Refers to the cells that line the internal and external surfaces of the body. [NIH]

Epithelial Cells: Cells that line the inner and outer surfaces of the body. [NIH]

Epithelium: One or more layers of epithelial cells, supported by the basal lamina, which covers the inner or outer surfaces of the body. [NIH]

Epitope: A molecule or portion of a molecule capable of binding to the combining site of an antibody. For every given antigenic determinant, the body can construct a variety of antibody-combining sites, some of which fit almost perfectly, and others which barely fit. [NIH]

Epoetin alfa: A colony-stimulating factor that is made in the laboratory. It increases the production of red blood cells. [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]

Erythrocyte Membrane: The semipermeable outer portion of the red corpuscle. It is known as a 'ghost' after hemolysis. [NIH]

Erythrocytes: Red blood cells. Mature erythrocytes are non-nucleated, biconcave disks containing hemoglobin whose function is to transport oxygen. [NIH]

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]

Esophageal: Having to do with the esophagus, the muscular tube through which food passes from the throat to the stomach. [NIH]

Esophageal Varices: Stretched veins in the esophagus that occur when the liver is not working properly. If the veins burst, the bleeding can cause death. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Essential Tremor: A rhythmic, involuntary, purposeless, oscillating movement resulting from the alternate contraction and relaxation of opposing groups of muscles. [NIH]

Estrogen: One of the two female sex hormones. [NIH]

Ethnic Groups: A group of people with a common cultural heritage that sets them apart from others in a variety of social relationships. [NIH]

Ethylmaleimide: A sulfhydryl reagent that is widely used in experimental biochemical studies. [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]

Excipient: Any more or less inert substance added to a prescription in order to confer a suitable consistency or form to the drug; a vehicle. [EU]

Excrete: To get rid of waste from the body. [NIH]

Exocrine: Secreting outwardly, via a duct. [EU]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Exon: The part of the DNA that encodes the information for the actual amino acid sequence of the protein. In many eucaryotic genes, the coding sequences consist of a series of exons alternating with intron sequences. [NIH]

Extensor: A muscle whose contraction tends to straighten a limb; the antagonist of a flexor. [NIH]

Extracellular: Outside a cell or cells. [EU]

Extracellular Matrix: A meshwork-like substance found within the extracellular space and in association with the basement membrane of the cell surface. It promotes cellular proliferation and provides a supporting structure to which cells or cell lysates in culture dishes adhere. [NIH]

Extracellular Matrix Proteins: Macromolecular organic compounds that contain carbon, hydrogen, oxygen, nitrogen, and usually, sulfur. These macromolecules (proteins) form an intricate meshwork in which cells are embedded to construct tissues. Variations in the relative types of macromolecules and their organization determine the type of extracellular matrix, each adapted to the functional requirements of the tissue. The two main classes of macromolecules that form the extracellular matrix are: glycosaminoglycans, usually linked to proteins (proteoglycans), and fibrous proteins (e.g., collagen, elastin, fibronectins and laminin). [NIH]

Extracellular Space: Interstitial space between cells, occupied by fluid as well as amorphous and fibrous substances. [NIH]

Extraction: The process or act of pulling or drawing out. [EU]

Extrapyramidal: Outside of the pyramidal tracts. [EU]

Extrarenal: Outside of the kidney. [EU]

Facial: Of or pertaining to the face. [EU]

Faecal: Pertaining to or of the nature of feces. [EU]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Fat: Total lipids including phospholipids. [NIH]

Fatigue: The state of weariness following a period of exertion, mental or physical, characterized by a decreased capacity for work and reduced efficiency to respond to stimuli. [NIH]

Fatty acids: A major component of fats that are used by the body for energy and tissue development. [NIH]

Febrile: Pertaining to or characterized by fever. [EU]

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]

Fetal Development: Morphologic and physiologic growth and development of the mammalian embryo or fetus. [NIH]

Fetus: The developing offspring from 7 to 8 weeks after conception until birth. [NIH]

Fibrillation: A small, local, involuntary contraction of muscle, invisible under the skin, resulting from spontaneous activation of single muscle cells or muscle fibres. [EU]

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]

Fibula: The bone of the lower leg lateral to and smaller than the tibia. In proportion to its length, it is the most slender of the long bones. [NIH]

Filtration: The passage of a liquid through a filter, accomplished by gravity, pressure, or vacuum (suction). [EU]

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]

Fistula: Abnormal communication most commonly seen between two internal organs, or between an internal organ and the surface of the body. [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]

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]

Foramen: A natural hole of perforation, especially one in a bone. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Freeze-dried: A method used to dry substances, such as food, to make them last longer. The substance is frozen and then dried in a vacuum. [NIH]

Fructose: A type of sugar found in many fruits and vegetables and in honey. Fructose is used to sweeten some diet foods. It is considered a nutritive sweetener because it has

calories. [NIH]

Fungi: A kingdom of eukaryotic, heterotrophic organisms that live as saprobes or parasites, including mushrooms, yeasts, smuts, molds, etc. They reproduce either sexually or asexually, and have life cycles that range from simple to complex. Filamentous fungi refer to those that grow as multicelluar colonies (mushrooms and molds). [NIH]

Gallbladder: The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

Gap Junctions: Connections between cells which allow passage of small molecules and electric current. Gap junctions were first described anatomically as regions of close apposition between cells with a narrow (1-2 nm) gap between cell membranes. The variety in the properties of gap junctions is reflected in the number of connexins, the family of proteins which form the junctions. [NIH]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gas exchange: Primary function of the lungs; transfer of oxygen from inhaled air into the blood and of carbon dioxide from the blood into the lungs. [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gastroenterologist: A doctor who specializes in diagnosing and treating disorders of the digestive system. [NIH]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gelatin: A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [NIH]

Gene: The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein. [NIH]

Gene Deletion: A genetic rearrangement through loss of segments of DNA or RNA, bringing sequences which are normally separated into close proximity. This deletion may be detected using cytogenetic techniques and can also be inferred from the phenotype, indicating a deletion at one specific locus. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Gene Targeting: The integration of exogenous DNA into the genome of an organism at sites where its expression can be suitably controlled. This integration occurs as a result of homologous recombination. [NIH]

Genetic Code: The specifications for how information, stored in nucleic acid sequence (base sequence), is translated into protein sequence (amino acid sequence). The start, stop, and order of amino acids of a protein is specified by consecutive triplets of nucleotides called codons (codon). [NIH]

Genetic Engineering: Directed modification of the gene complement of a living organism by such techniques as altering the DNA, substituting genetic material by means of a virus, transplanting whole nuclei, transplanting cell hybrids, etc. [NIH]

Genetic Predisposition to Disease: A latent susceptibility to disease at the genetic level, which may be activated under certain conditions. [NIH]

Genetic testing: Analyzing DNA to look for a genetic alteration that may indicate an increased risk for developing a specific disease or disorder. [NIH]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genital: Pertaining to the genitalia. [EU]

Genitourinary: Pertaining to the genital and urinary organs; urogenital; urinosexual. [EU]

Genitourinary system: The parts of the body that play a role in reproduction, getting rid of waste products in the form of urine, or both. [NIH]

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]

Germ Cells: The reproductive cells in multicellular organisms. [NIH]

Germ-free: Free of bacteria, disease-causing viruses, and other organisms that can cause infection. [NIH]

Gestation: The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

Gestational: Psychosis attributable to or occurring during pregnancy. [NIH]

Giant Cells: Multinucleated masses produced by the fusion of many cells; often associated with viral infections. In AIDS, they are induced when the envelope glycoprotein of the HIV virus binds to the CD4 antigen of uninfected neighboring T4 cells. The resulting syncytium leads to cell death and thus may account for the cytopathic effect of the virus. [NIH]

Gland: An organ that produces and releases one or more substances for use in the body. Some glands produce fluids that affect tissues or organs. Others produce hormones or participate in blood production. [NIH]

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]

Glomerulonephritis, Membranous: A disease of the glomerulus manifested clinically by proteinuria, and sometimes by other features of the nephrotic syndrome. It is histologically characterized by deposits in the glomerular capillary wall between the epithelial cell and the basement membrane and a thickening of the membrane. Also characteristic are outward projections of the membrane between the epithelial deposits in the form of "spikes". There is some agreement that the deposits are antigen-antibody complexes. [NIH]

Glomerulosclerosis: Scarring of the glomeruli. It may result from diabetes mellitus (diabetic glomerulosclerosis) or from deposits in parts of the glomerulus (focal segmental glomerulosclerosis). The most common signs of glomerulosclerosis are proteinuria and kidney failure. [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]

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]

Glutamate: Excitatory neurotransmitter of the brain. [NIH]

Glutamic Acid: A non-essential amino acid naturally occurring in the L-form. Glutamic acid (glutamate) is the most common excitatory neurotransmitter in the central nervous system. [NIH]

Gluten: The protein of wheat and other grains which gives to the dough its tough elastic character. [EU]

Glycine: A non-essential amino acid. It is found primarily in gelatin and silk fibroin and used therapeutically as a nutrient. It is also a fast inhibitory neurotransmitter. [NIH]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Glycosaminoglycans: Heteropolysaccharides which contain an N-acetylated hexosamine in a characteristic repeating disaccharide unit. The repeating structure of each disaccharide involves alternate 1,4- and 1,3-linkages consisting of either N-acetylglucosamine or N-acetylgalactosamine. [NIH]

Glycoside: Any compound that contains a carbohydrate molecule (sugar), particularly any such natural product in plants, convertible, by hydrolytic cleavage, into sugar and a nonsugar component (aglycone), and named specifically for the sugar contained, as glucoside (glucose), pentoside (pentose), fructoside (fructose) etc. [EU]

Glycosidic: Formed by elimination of water between the anomeric hydroxyl of one sugar and a hydroxyl of another sugar molecule. [NIH]

Glycosylation: The chemical or biochemical addition of carbohydrate or glycosyl groups to other chemicals, especially peptides or proteins. Glycosyl transferases are used in this biochemical reaction. [NIH]

Goats: Any of numerous agile, hollow-horned ruminants of the genus Capra, closely related to the sheep. [NIH]

Gonadal: Pertaining to a gonad. [EU]

Gout: Hereditary metabolic disorder characterized by recurrent acute arthritis, hyperuricemia and deposition of sodium urate in and around the joints, sometimes with formation of uric acid calculi. [NIH]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

Gp120: 120-kD HIV envelope glycoprotein which is involved in the binding of the virus to its membrane receptor, the CD4 molecule, found on the surface of certain cells in the body. [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

Graft Rejection: An immune response with both cellular and humoral components, directed against an allogeneic transplant, whose tissue antigens are not compatible with those of the recipient. [NIH]

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]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Grasses: A large family, Gramineae, of narrow-leaved herbaceous monocots. Many grasses produce highly allergenic pollens and are hosts to cattle parasites and toxic fungi. [NIH]

Growth: The progressive development of a living being or part of an organism from its earliest stage to maturity. [NIH]

Growth factors: Substances made by the body that function to regulate cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy. [NIH]

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]

Habitual: Of the nature of a habit; according to habit; established by or repeated by force of habit, customary. [EU]

Haematoma: A localized collection of blood, usually clotted, in an organ, space, or tissue, due to a break in the wall of a blood vessel. [EU]

Haematuria: Blood in the urine. [EU]

Haemodialysis: The removal of certain elements from the blood by virtue of the difference in the rates of their diffusion through a semipermeable membrane, e.g., by means of a haemodialyzer. [EU]

Haemorrhage: The escape of blood from the vessels; bleeding. Small haemorrhages are classified according to size as petechiae (very small), purpura (up to 1 cm), and ecchymoses (larger). The massive accumulation of blood within a tissue is called a haematoma. [EU]

Haptens: Small antigenic determinants capable of eliciting an immune response only when coupled to a carrier. Haptens bind to antibodies but by themselves cannot elicit an antibody

response. [NIH]

Headache: Pain in the cranial region that may occur as an isolated and benign symptom or as a manifestation of a wide variety of conditions including subarachnoid hemorrhage; craniocerebral trauma; central nervous system infections; intracranial hypertension; and other disorders. In general, recurrent headaches that are not associated with a primary disease process are referred to as headache disorders (e.g., migraine). [NIH]

Health Care Costs: The actual costs of providing services related to the delivery of health care, including the costs of procedures, therapies, and medications. It is differentiated from health expenditures, which refers to the amount of money paid for the services, and from fees, which refers to the amount charged, regardless of cost. [NIH]

Health Expenditures: The amounts spent by individuals, groups, nations, or private or public organizations for total health care and/or its various components. These amounts may or may not be equivalent to the actual costs (health care costs) and may or may not be shared among the patient, insurers, and/or employers. [NIH]

Health Planning: Planning for needed health and/or welfare services and facilities. [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]

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]

Heartbeat: One complete contraction of the heart. [NIH]

Heartburn: Substernal pain or burning sensation, usually associated with regurgitation of gastric juice into the esophagus. [NIH]

Hematocrit: Measurement of the volume of packed red cells in a blood specimen by centrifugation. The procedure is performed using a tube with graduated markings or with automated blood cell counters. It is used as an indicator of erythrocyte status in disease. For example, anemia shows a low hematocrit, polycythemia, high values. [NIH]

Hematopoietic Stem Cells: Progenitor cells from which all blood cells derive. [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]

Hemodiafiltration: The combination of hemodialysis and hemofiltration either simultaneously or sequentially. Convective transport (hemofiltration) may be better for removal of larger molecular weight substances and diffusive transport (hemodialysis) for smaller molecular weight solutes. [NIH]

Hemodialysis: The use of a machine to clean wastes from the blood after the kidneys have failed. The blood travels through tubes to a dialyzer, which removes wastes and extra fluid. The cleaned blood then flows through another set of tubes back into the body. [NIH]

Hemodynamics: The movements of the blood and the forces involved in systemic or regional blood circulation. [NIH]

Hemofiltration: Extracorporeal ultrafiltration technique without hemodialysis for treatment of fluid overload and electrolyte disturbances affecting renal, cardiac, or pulmonary function. [NIH]

Hemoglobin: One of the fractions of glycosylated hemoglobin A1c. Glycosylated hemoglobin is formed when linkages of glucose and related monosaccharides bind to

hemoglobin A and its concentration represents the average blood glucose level over the previous several weeks. HbA1c levels are used as a measure of long-term control of plasma glucose (normal, 4 to 6 percent). In controlled diabetes mellitus, the concentration of glycosylated hemoglobin A is within the normal range, but in uncontrolled cases the level may be 3 to 4 times the normal conentration. Generally, complications are substantially lower among patients with Hb levels of 7 percent or less than in patients with HbA1c levels of 9 percent or more. [NIH]

Hemoglobin C: A commonly occurring abnormal hemoglobin in which lysine replaces a glutamic acid residue at the sixth position of the beta chains. It results in reduced plasticity of erythrocytes. [NIH]

Hemoglobinuria: The presence of free hemoglobin in the urine. [NIH]

Hemolysis: The destruction of erythrocytes by many different causal agents such as antibodies, bacteria, chemicals, temperature, and changes in tonicity. [NIH]

Hemolytic: A disease that affects the blood and blood vessels. It destroys red blood cells, cells that cause the blood to clot, and the lining of blood vessels. HUS is often caused by the Escherichia coli bacterium in contaminated food. People with HUS may develop acute renal failure. [NIH]

Hemolytic-Uremic Syndrome: Syndrome of hemolytic anemia, thrombocytopenia, and acute renal failure, with pathological finding of thrombotic microangiopathy in kidney and renal cortical necrosis. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Heparan Sulfate Proteoglycan: A substance released by astrocytes, which is critical in stopping nervous fibers in their tracks. [NIH]

Heparin: Heparinic acid. A highly acidic mucopolysaccharide formed of equal parts of sulfated D-glucosamine and D-glucuronic acid with sulfaminic bridges. The molecular weight ranges from six to twenty thousand. Heparin occurs in and is obtained from liver, lung, mast cells, etc., of vertebrates. Its function is unknown, but it is used to prevent blood clotting in vivo and vitro, in the form of many different salts. [NIH]

Hepatic: Refers to the liver. [NIH]

Hepatic Encephalopathy: A condition that may cause loss of consciousness and coma. It is usually the result of advanced liver disease. Also called hepatic coma. [NIH]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatocyte: A liver cell. [NIH]

Hepatocyte Growth Factor: Multifunctional growth factor which regulates both cell growth and cell motility. It exerts a strong mitogenic effect on hepatocytes and primary epithelial cells. Its receptor is proto-oncogene protein C-met. [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]

Hernia: Protrusion of a loop or knuckle of an organ or tissue through an abnormal opening. [NIH]

Heteroduplex Analysis: A method of detecting gene mutation by mixing PCR-amplified mutant and wild-type DNA followed by denaturation and reannealing. The resultant products are resolved by gel electrophoresis, with single base substitutions detectable under

optimal electrophoretic conditions and gel formulations. Large base pair mismatches may also be analyzed by using electron microscopy to visualize heteroduplex regions. [NIH]

Heterogeneity: The property of one or more samples or populations which implies that they are not identical in respect of some or all of their parameters, e. g. heterogeneity of variance. [NIH]

Heterogenic: Derived from a different source or species. Also called heterogenous. [NIH]

Heterogenous: Derived from a different source or species. Also called heterogenic. [NIH]

Heterozygotes: Having unlike alleles at one or more corresponding loci on homologous chromosomes. [NIH]

Histamine: 1H-Imidazole-4-ethanamine. A depressor amine derived by enzymatic decarboxylation of histidine. It is a powerful stimulant of gastric secretion, a constrictor of bronchial smooth muscle, a vasodilator, and also a centrally acting neurotransmitter. [NIH]

Histidine: An essential amino acid important in a number of metabolic processes. It is required for the production of histamine. [NIH]

Histology: The study of tissues and cells under a microscope. [NIH]

Homeostasis: The processes whereby the internal environment of an organism tends to remain balanced and stable. [NIH]

Homodimer: Protein-binding "activation domains" always combine with identical proteins. [NIH]

Homogeneous: Consisting of or composed of similar elements or ingredients; of a uniform quality throughout. [EU]

Homologous: Corresponding in structure, position, origin, etc., as (a) the feathers of a bird and the scales of a fish, (b) antigen and its specific antibody, (c) allelic chromosomes. [EU]

Homozygote: An individual in which both alleles at a given locus are identical. [NIH]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Hormone therapy: Treatment of cancer by removing, blocking, or adding hormones. Also called endocrine therapy. [NIH]

Host: Any animal that receives a transplanted graft. [NIH]

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]

Hybridization: The genetic process of crossbreeding to produce a hybrid. Hybrid nucleic acids can be formed by nucleic acid hybridization of DNA and RNA molecules. Protein hybridization allows for hybrid proteins to be formed from polypeptide chains. [NIH]

Hybridomas: Cells artificially created by fusion of activated lymphocytes with neoplastic cells. The resulting hybrid cells are cloned and produce pure or "monoclonal" antibodies or T-cell products, identical to those produced by the immunologically competent parent, and continually grow and divide as the neoplastic parent. [NIH]

Hydration: Combining with water. [NIH]

Hydrogen: The first chemical element in the periodic table. It has the atomic symbol H, atomic number 1, and atomic weight 1. It exists, under normal conditions, as a colorless, odorless, tasteless, diatomic gas. Hydrogen ions are protons. Besides the common H1 isotope, hydrogen exists as the stable isotope deuterium and the unstable, radioactive isotope tritium. [NIH]

Hydrogen Peroxide: A strong oxidizing agent used in aqueous solution as a ripening agent, bleach, and topical anti-infective. It is relatively unstable and solutions deteriorate over time unless stabilized by the addition of acetanilide or similar organic materials. [NIH]

Hydrolysis: The process of cleaving a chemical compound by the addition of a molecule of water. [NIH]

Hydronephrosis: Abnormal enlargement of a kidney, which may be caused by blockage of the ureter (such as by a kidney stone) or chronic kidney disease that prevents urine from draining into the bladder. [NIH]

Hydrophobic: Not readily absorbing water, or being adversely affected by water, as a hydrophobic colloid. [EU]

Hydroxylysine: A hydroxylated derivative of the amino acid lysine that is present in certain collagens. [NIH]

Hydroxyproline: A hydroxylated form of the imino acid proline. A deficiency in ascorbic acid can result in impaired hydroxyproline formation. [NIH]

Hypercholesterolemia: Abnormally high levels of cholesterol in the blood. [NIH]

Hyperglycemia: Abnormally high blood sugar. [NIH]

Hyperlipidemia: An excess of lipids in the blood. [NIH]

Hyperlipoproteinemia: Metabolic disease characterized by elevated plasma cholesterol and/or triglyceride levels. The inherited form is attributed to a single gene mechanism. [NIH]

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]

Hypertension, Renal: Hypertension due to renal diseases, especially chronic parenchymal disease. Hypertension as a result of compression or obstruction of the renal artery or its branches is hypertension, renovascular. [NIH]

Hypertension, Renovascular: Hypertension due to compression or obstruction of the renal artery or its branches. [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]

Hypoplasia: Incomplete development or underdevelopment of an organ or tissue. [EU]

Hypotension: Abnormally low blood pressure. [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]

Ice Cream: A frozen dairy food made from cream or butterfat, milk, sugar, and flavorings. Frozen custard and French-type ice creams also contain eggs. [NIH]

Id: The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Idiopathic: Describes a disease of unknown cause. [NIH]

Ifosfamide: Positional isomer of cyclophosphamide which is active as an alkylating agent and an immunosuppressive agent. [NIH]

Immersion: The placing of a body or a part thereof into a liquid. [NIH]

Immune function: Production and action of cells that fight disease or infection. [NIH]

Immune response: The activity of the immune system against foreign substances (antigens). [NIH]

Immune system: The organs, cells, and molecules responsible for the recognition and disposal of foreign ("non-self") material which enters the body. [NIH]

Immunity: Nonsusceptibility to the invasive or pathogenic effects of foreign microorganisms or to the toxic effect of antigenic substances. [NIH]

Immunization: Deliberate stimulation of the host's immune response. Active immunization involves administration of antigens or immunologic adjuvants. Passive immunization involves administration of immune sera or lymphocytes or their extracts (e.g., transfer factor, immune RNA) or transplantation of immunocompetent cell producing tissue (thymus or bone marrow). [NIH]

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]

Immunohistochemistry: Histochemical localization of immunoreactive substances using labeled antibodies as reagents. [NIH]

Immunologic: The ability of the antibody-forming system to recall a previous experience with an antigen and to respond to a second exposure with the prompt production of large amounts of antibody. [NIH]

Immunology: The study of the body's immune system. [NIH]

Immunosuppressant: An agent capable of suppressing immune responses. [EU]

Immunosuppressive: Describes the ability to lower immune system responses. [NIH]

Immunosuppressive Agents: Agents that suppress immune function by one of several mechanisms of action. Classical cytotoxic immunosuppressants act by inhibiting DNA synthesis. Others may act through activation of suppressor T-cell populations or by inhibiting the activation of helper cells. While immunosuppression has been brought about in the past primarily to prevent rejection of transplanted organs, new applications involving mediation of the effects of interleukins and other cytokines are emerging. [NIH]

Immunosuppressive therapy: Therapy used to decrease the body's immune response, such as drugs given to prevent transplant rejection. [NIH]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

Impotence: The inability to perform sexual intercourse. [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]

Incontinence: Inability to control the flow of urine from the bladder (urinary incontinence) or the escape of stool from the rectum (fecal incontinence). [NIH]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

Indigestion: Poor digestion. Symptoms include heartburn, nausea, bloating, and gas. Also called dyspepsia. [NIH]

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 Behavior: Any observable response or action of a neonate or infant up through the age of 23 months. [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]

Infertility: The diminished or absent ability to conceive or produce an offspring while sterility is the complete inability to conceive or produce an offspring. [NIH]

Infestation: Parasitic attack or subsistence on the skin and/or its appendages, as by insects, mites, or ticks; sometimes used to denote parasitic invasion of the organs and tissues, as by helminths. [NIH]

Infiltration: The diffusion or accumulation in a tissue or cells of substances not normal to it or in amounts of the normal. Also, the material so accumulated. [EU]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Inflammatory bowel disease: A general term that refers to the inflammation of the colon and rectum. Inflammatory bowel disease includes ulcerative colitis and Crohn's disease. [NIH]

Infusion: A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

Ingestion: Taking into the body by mouth [NIH]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

Initiator: A chemically reactive substance which may cause cell changes if ingested, inhaled or absorbed into the body; the substance may thus initiate a carcinogenic process. [NIH]

Inorganic: Pertaining to substances not of organic origin. [EU]

Inotropic: Affecting the force or energy of muscular contractions. [EU]

Insight: The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Insomnia: Difficulty in going to sleep or getting enough sleep. [NIH]

Instillation: . [EU]

Insulator: Material covering the metal conductor of the lead. It is usually polyurethane or silicone. [NIH]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Insulin-dependent diabetes mellitus: A disease characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Autoimmune, genetic, and environmental factors are involved in the development of type I diabetes. [NIH]

Insulin-like: Muscular growth factor. [NIH]

Integrins: A family of transmembrane glycoproteins consisting of noncovalent heterodimers. They interact with a wide variety of ligands including extracellular matrix glycoproteins, complement, and other cells, while their intracellular domains interact with the cytoskeleton. The integrins consist of at least three identified families: the cytoadhesin receptors, the leukocyte adhesion receptors, and the very-late-antigen receptors. Each family contains a common beta-subunit combined with one or more distinct alpha-subunits. These receptors participate in cell-matrix and cell-cell adhesion in many physiologically important processes, including embryological development, hemostasis, thrombosis, wound healing, immune and nonimmune defense mechanisms, and oncogenic transformation. [NIH]

Interferon: A biological response modifier (a substance that can improve the body's natural response to disease). Interferons interfere with the division of cancer cells and can slow tumor growth. There are several types of interferons, including interferon-alpha, -beta, and -gamma. These substances are normally produced by the body. They are also made in the laboratory for use in treating cancer and other diseases. [NIH]

Interferon-alpha: One of the type I interferons produced by peripheral blood leukocytes or

lymphoblastoid cells when exposed to live or inactivated virus, double-stranded RNA, or bacterial products. It is the major interferon produced by virus-induced leukocyte cultures and, in addition to its pronounced antiviral activity, it causes activation of NK cells. [NIH]

Interleukin-1: A soluble factor produced by monocytes, macrophages, and other cells which activates T-lymphocytes and potentiates their response to mitogens or antigens. IL-1 consists of two distinct forms, IL-1 alpha and IL-1 beta which perform the same functions but are distinct proteins. The biological effects of IL-1 include the ability to replace macrophage requirements for T-cell activation. The factor is distinct from interleukin-2. [NIH]

Interleukin-2: Chemical mediator produced by activated T lymphocytes and which regulates the proliferation of T cells, as well as playing a role in the regulation of NK cell activity. [NIH]

Interleukin-6: Factor that stimulates the growth and differentiation of human B-cells and is also a growth factor for hybridomas and plasmacytomas. It is produced by many different cells including T-cells, monocytes, and fibroblasts. [NIH]

Interleukins: Soluble factors which stimulate growth-related activities of leukocytes as well as other cell types. They enhance cell proliferation and differentiation, DNA synthesis, secretion of other biologically active molecules and responses to immune and inflammatory stimuli. [NIH]

Intermediate Filaments: Cytoplasmic filaments intermediate in diameter (about 10 nanometers) between the microfilaments and the microtubules. They may be composed of any of a number of different proteins and form a ring around the cell nucleus. [NIH]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

Internal Medicine: A medical specialty concerned with the diagnosis and treatment of diseases of the internal organ systems of adults. [NIH]

Interstitial: Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

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]

Intracellular Membranes: Membranes of subcellular structures. [NIH]

Intracranial Aneurysm: A saclike dilatation of the walls of a blood vessel, usually an artery. [NIH]

Intravenous: IV. Into a vein. [NIH]

Intravenous pyelography: IVP. X-ray study of the kidneys, ureters, and bladder. The x-rays are taken after a dye is injected into a blood vessel. The dye is concentrated in the urine, which outlines the kidneys, ureters, and bladder on the x-rays. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

Introns: Non-coding, intervening sequences of DNA that are transcribed, but are removed from within the primary gene transcript and rapidly degraded during maturation of messenger RNA. Most genes in the nuclei of eukaryotes contain introns, as do mitochondrial and chloroplast genes. [NIH]

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]

Iodine: A nonmetallic element of the halogen group that is represented by the atomic symbol I, atomic number 53, and atomic weight of 126.90. It is a nutritionally essential element, especially important in thyroid hormone synthesis. In solution, it has anti-infective properties and is used topically. [NIH]

Iohexol: An effective non-ionic, water-soluble contrast agent which is used in myelography, arthrography, nephroangiography, arteriography, and other radiographic procedures. Its low systemic toxicity is the combined result of low chemotoxicity and low osmolality. [NIH]

Ion Channels: Gated, ion-selective glycoproteins that traverse membranes. The stimulus for channel gating can be a membrane potential, drug, transmitter, cytoplasmic messenger, or a mechanical deformation. Ion channels which are integral parts of ionotropic neurotransmitter receptors are not included. [NIH]

Ion Transport: The movement of ions across energy-transducing cell membranes. Transport can be active or passive. Passive ion transport (facilitated diffusion) derives its energy from the concentration gradient of the ion itself and allows the transport of a single solute in one direction (uniport). Active ion transport is usually coupled to an energy-yielding chemical or photochemical reaction such as ATP hydrolysis. This form of primary active transport is called an ion pump. Secondary active transport utilizes the voltage and ion gradients produced by the primary transport to drive the cotransport of other ions or molecules. These may be transported in the same (symport) or opposite (antiport) direction. [NIH]

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]

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]

IVP: Intravenous pyelogram or intravenous pyelography (in-tra-VEE-nus PYE-el-o-gram or pye-LAH-gra-fee). A series of x-rays of the kidneys, ureters, and bladder. The x-rays are taken after a dye is injected into a blood vessel. The dye is concentrated in the urine, which outlines the kidneys, ureters, and bladder on the x-rays. [NIH]

Joint: The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

Kallikrein-Kinin System: A system produced in the distal nephron of the kidney. Its components are kallikrein, kinins, kininase I and II, and enkephalinase. It is involved in mediation and modulation of the renin-angiotensin-aldosterone system, prostaglandins, vasopressins, and in the regulation of sodium-water balance, renal hemodynamics, and particularly blood pressure. The system participates in the control of renal functions and the physiopathology of renal diseases. [NIH]

Kanamycin: Antibiotic complex produced by Streptomyces kanamyceticus from Japanese soil. Comprises 3 components: kanamycin A, the major component, and kanamycins B and

C, the minor components. [NIH]

Kb: A measure of the length of DNA fragments, 1 Kb = 1000 base pairs. The largest DNA fragments are up to 50 kilobases long. [NIH]

Kidney Disease: Any one of several chronic conditions that are caused by damage to the cells of the kidney. People who have had diabetes for a long time may have kidney damage. Also called nephropathy. [NIH]

Kidney Failure: The inability of a kidney to excrete metabolites at normal plasma levels under conditions of normal loading, or the inability to retain electrolytes under conditions of normal intake. In the acute form (kidney failure, acute), it is marked by uremia and usually by oliguria or anuria, with hyperkalemia and pulmonary edema. The chronic form (kidney failure, chronic) is irreversible and requires hemodialysis. [NIH]

Kidney Failure, Acute: A clinical syndrome characterized by a sudden decrease in glomerular filtration rate, often to values of less than 1 to 2 ml per minute. It is usually associated with oliguria (urine volumes of less than 400 ml per day) and is always associated with biochemical consequences of the reduction in glomerular filtration rate such as a rise in blood urea nitrogen (BUN) and serum creatinine concentrations. [NIH]

Kidney Failure, Chronic: An irreversible and usually progressive reduction in renal function in which both kidneys have been damaged by a variety of diseases to the extent that they are unable to adequately remove the metabolic products from the blood and regulate the body's electrolyte composition and acid-base balance. Chronic kidney failure requires hemodialysis or surgery, usually kidney transplantation. [NIH]

Kidney stone: A stone that develops from crystals that form in urine and build up on the inner surfaces of the kidney, in the renal pelvis, or in the ureters. [NIH]

Kidney Transplantation: The transference of a kidney from one human or animal to another. [NIH]

Kinesin: A microtubule-associated mechanical adenosine triphosphatase, that uses the energy of ATP hydrolysis to move organelles along microtubules toward the plus end of the microtubule. The protein is found in squid axoplasm, optic lobes, and in bovine brain. Bovine kinesin is a heterotetramer composed of two heavy (120 kDa) and two light (62 kDa) chains. EC 3.6.1.-. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Labile: 1. Gliding; moving from point to point over the surface; unstable; fluctuating. 2. Chemically unstable. [EU]

Laminin: Large, noncollagenous glycoprotein with antigenic properties. It is localized in the basement membrane lamina lucida and functions to bind epithelial cells to the basement membrane. Evidence suggests that the protein plays a role in tumor invasion. [NIH]

Lamivudine: A reverse transcriptase inhibitor and zalcitabine analog in which a sulfur atom replaces the 3' carbon of the pentose ring. It is used to treat HIV disease. [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]

Lectin: A complex molecule that has both protein and sugars. Lectins are able to bind to the outside of a cell and cause biochemical changes in it. Lectins are made by both animals and plants. [NIH]

Leiomyoma: A benign tumor derived from smooth muscle tissue, also known as a fibroid tumor. They rarely occur outside of the uterus and the gastrointestinal tract but can occur in the skin and subcutaneous tissues, probably arising from the smooth muscle of small blood vessels in these tissues. [NIH]

Leprosy: A chronic granulomatous infection caused by Mycobacterium leprae. The granulomatous lesions are manifested in the skin, the mucous membranes, and the peripheral nerves. Two polar or principal types are lepromatous and tuberculoid. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Lethal: Deadly, fatal. [EU]

Leucine: An essential branched-chain amino acid important for hemoglobin formation. [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]

Leukopenia: A condition in which the number of leukocytes (white blood cells) in the blood is reduced. [NIH]

Library Services: Services offered to the library user. They include reference and circulation. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and strengthen joints. [EU]

Ligands: A RNA simulation method developed by the MIT. [NIH]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Linkage Disequilibrium: Nonrandom association of linked genes. This is the tendency of the alleles of two separate but already linked loci to be found together more frequently than would be expected by chance alone. [NIH]

Lipid: Fat. [NIH]

Lipid 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]

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]

Localization: The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

Localized: Cancer which has not metastasized yet. [NIH]

Locomotion: Movement or the ability to move from one place or another. It can refer to humans, vertebrate or invertebrate animals, and microorganisms. [NIH]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

Long-Term Care: Care over an extended period, usually for a chronic condition or disability, requiring periodic, intermittent, or continuous care. [NIH]

Loop: A wire usually of platinum bent at one end into a small loop (usually 4 mm inside diameter) and used in transferring microorganisms. [NIH]

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]

Lucida: An instrument, invented by Wollaton, consisting essentially of a prism or a mirror through which an object can be viewed so as to appear on a plane surface seen in direct view and on which the outline of the object may be traced. [NIH]

Lumbar: Pertaining to the loins, the part of the back between the thorax and the pelvis. [EU]

Lupus: A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

Lupus Nephritis: Glomerulonephritis associated with systemic lupus erythematosus. It is classified into four histologic types: mesangial, focal, diffuse, and membranous. [NIH]

Lymph: The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

Lymph node: A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Also known as a lymph gland. Lymph nodes are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic fluid (lymph). [NIH]

Lymphatic: The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells.

These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphokines: Soluble protein factors generated by activated lymphocytes that affect other cells, primarily those involved in cellular immunity. [NIH]

Lymphoma: A general term for various neoplastic diseases of the lymphoid tissue. [NIH]

Lysine: An essential amino acid. It is often added to animal feed. [NIH]

Macrophage: A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells. [NIH]

Macrophage Activation: The process of altering the morphology and functional activity of macrophages so that they become avidly phagocytic. It is initiated by lymphokines, such as the macrophage activation factor (MAF) and the macrophage migration-inhibitory factor (MMIF), immune complexes, C3b, and various peptides, polysaccharides, and immunologic adjuvants. [NIH]

Macula: A stain, spot, or thickening. Often used alone to refer to the macula retinae. [EU]

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]

Major Histocompatibility Complex: The genetic region which contains the loci of genes which determine the structure of the serologically defined (SD) and lymphocyte-defined (LD) transplantation antigens, genes which control the structure of the immune response-associated (Ia) antigens, the immune response (Ir) genes which control the ability of an animal to respond immunologically to antigenic stimuli, and genes which determine the structure and/or level of the first four components of complement. [NIH]

Malabsorption: Impaired intestinal absorption of nutrients. [EU]

Malformation: A morphologic defect resulting from an intrinsically abnormal developmental process. [EU]

Malignancy: A cancerous tumor that can invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

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]

Manic: Affected with mania. [EU]

Manic-depressive psychosis: One of a group of psychotic reactions, fundamentally marked

by severe mood swings and a tendency to remission and recurrence. [NIH]

Mean blood pressure: The average blood pressure, taking account of the rise and fall that occurs with each heartbeat. It is often estimated by multiplying the diastolic pressure by two, adding the systolic pressure, and then dividing this sum by three. [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]

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 Staff: Professional medical personnel who provide care to patients in an organized facility, institution or agency. [NIH]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Medullary: Pertaining to the marrow or to any medulla; resembling marrow. [EU]

Megaloblastic: A large abnormal red blood cell appearing in the blood in pernicious anaemia. [EU]

Meiosis: A special method of cell division, occurring in maturation of the germ cells, by means of which each daughter nucleus receives half the number of chromosomes characteristic of the somatic cells of the species. [NIH]

Melanin: The substance that gives the skin its color. [NIH]

Melanocytes: Epidermal dendritic pigment cells which control long-term morphological color changes by alteration in their number or in the amount of pigment they produce and store in the pigment containing organelles called melanosomes. Melanophores are larger cells which do not exist in mammals. [NIH]

Melanoma: A form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

Membrane Fusion: The adherence of cell membranes, intracellular membranes, or artifical membrane models of either to each other or to viruses, parasites, or interstitial particles through a variety of chemical and physical processes. [NIH]

Membrane Glycoproteins: Glycoproteins found on the membrane or surface of cells. [NIH]

Membrane Proteins: Proteins which are found in membranes including cellular and intracellular membranes. They consist of two types, peripheral and integral proteins. They include most membrane-associated enzymes, antigenic proteins, transport proteins, and drug, hormone, and lectin receptors. [NIH]

Membranoproliferative: A disease that occurs primarily in children and young adults. Over time, inflammation leads to scarring in the glomeruli, causing proteinuria, hematuria, and sometimes chronic renal failure or end-stage renal disease. [NIH]

Memory: Complex mental function having four distinct phases: (1) memorizing or learning, (2) retention, (3) recall, and (4) recognition. Clinically, it is usually subdivided into immediate, recent, and remote memory. [NIH]

Meningeal: Refers to the meninges, the tissue covering the brain and spinal cord. [NIH]

Meninges: The three membranes that cover and protect the brain and spinal cord. [NIH]

Menopause: Permanent cessation of menstruation. [NIH]

Menstrual Cycle: The period of the regularly recurring physiologic changes in the endometrium occurring during the reproductive period in human females and some primates and culminating in partial sloughing of the endometrium (menstruation). [NIH]

Menstruation: The normal physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus. [NIH]

Mental Disorders: Psychiatric illness or diseases manifested by breakdowns in the adaptational process expressed primarily as abnormalities of thought, feeling, and behavior producing either distress or impairment of function. [NIH]

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]

Mesoderm: The middle germ layer of the embryo. [NIH]

Mesonephros: The excretory organ of the embryo, collective Wolffian tubules, which forms the urogenital fold from which the reproductive organs develop. The mesonephros is the permanent kidney in fish and amphibians, but atrophies in reptiles, birds, and mammals. [NIH]

Meta-Analysis: A quantitative method of combining the results of independent studies (usually drawn from the published literature) and synthesizing summaries and conclusions which may be used to evaluate therapeutic effectiveness, plan new studies, etc., with application chiefly in the areas of research and medicine. [NIH]

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]

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]

Metoprolol: Adrenergic beta-1-blocking agent with no stimulatory action. It is less bound to plasma albumin than alprenolol and may be useful in angina pectoris, hypertension, or cardiac arrhythmias. [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]

Microfilaments: The smallest of the cytoskeletal filaments. They are composed chiefly of actin. [NIH]

Microorganism: An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

Micro-organism: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microscopy: The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

Microtubules: Slender, cylindrical filaments found in the cytoskeleton of plant and animal cells. They are composed of the protein tubulin. [NIH]

Microvillus: A minute process or protrusion from the free surface of a cell. [EU]

Microwaves: That portion of the electromagnetic spectrum lying between UHF (ultrahigh frequency) radio waves and heat (infrared) waves. Microwaves are used to generate heat, especially in some types of diathermy. They may cause heat damage to tissues. [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]

Millimeter: A measure of length. A millimeter is approximately 26-times smaller than an inch. [NIH]

Mineralization: The action of mineralizing; the state of being mineralized. [EU]

Minocycline: A semisynthetic antibiotic effective against tetracycline-resistant staphylococcus infections. [NIH]

Minority Groups: A subgroup having special characteristics within a larger group, often bound together by special ties which distinguish it from the larger group. [NIH]

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]

Mitosis: A method of indirect cell division by means of which the two daughter nuclei normally receive identical complements of the number of chromosomes of the somatic cells of the species. [NIH]

Mitotic: Cell resulting from mitosis. [NIH]

Mitotic inhibitors: Drugs that kill cancer cells by interfering with cell division (mitostis). [NIH]

Mitral Valve: The valve between the left atrium and left ventricle of the heart. [NIH]

Mitral Valve Prolapse: Abnormal protrusion of one or both of the leaflets of the mitral valve into the left atrium during systole. This may be accompanied by mitral regurgitation, systolic murmur, nonejection click, or cardiac arrhythmia. [NIH]

Mobilization: The process of making a fixed part or stored substance mobile, as by

separating a part from surrounding structures to make it accessible for an operative procedure or by causing release into the circulation for body use of a substance stored in the body. [EU]

Modeling: A treatment procedure whereby the therapist presents the target behavior which the learner is to imitate and make part of his repertoire. [NIH]

Modification: A change in an organism, or in a process in an organism, that is acquired from its own activity or environment. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Molecule: A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

Monitor: An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

Monoclonal: An antibody produced by culturing a single type of cell. It therefore consists of a single species of immunoglobulin molecules. [NIH]

Monoclonal antibodies: Laboratory-produced substances that can locate and bind to cancer cells wherever they are in the body. Many monoclonal antibodies are used in cancer detection or therapy; each one recognizes a different protein on certain cancer cells. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to a tumor. [NIH]

Monocyte: A type of white blood cell. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Morphine: The principal alkaloid in opium and the prototype opiate analgesic and narcotic. Morphine has widespread effects in the central nervous system and on smooth muscle. [NIH]

Morphogenesis: The development of the form of an organ, part of the body, or organism. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Morphology: The science of the form and structure of organisms (plants, animals, and other forms of life). [NIH]

Motility: The ability to move spontaneously. [EU]

Motion Sickness: Sickness caused by motion, as sea sickness, train sickness, car sickness, and air sickness. [NIH]

Motor Activity: The physical activity of an organism as a behavioral phenomenon. [NIH]

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 Studies: Controlled studies which are planned and carried out by several cooperating institutions to assess certain variables and outcomes in specific patient populations, for example, a multicenter study of congenital anomalies in children. [NIH]

Multicenter study: A clinical trial that is carried out at more than one medical institution. [NIH]

Multicystic Dysplastic Kidney: A severe form of dysplasia where the kidney typically appears as a bunch of grapes without a reniform configuration or calyceal drainage system.

It occurs in-utero and is the most common form of nongenetic renal cystic disease. [NIH]

Multiple Myeloma: A malignant tumor of plasma cells usually arising in the bone marrow; characterized by diffuse involvement of the skeletal system, hyperglobulinemia, Bence-Jones proteinuria, and anemia. [NIH]

Multiple sclerosis: A disorder of the central nervous system marked by weakness, numbness, a loss of muscle coordination, and problems with vision, speech, and bladder control. Multiple sclerosis is thought to be an autoimmune disease in which the body's immune system destroys myelin. Myelin is a substance that contains both protein and fat (lipid) and serves as a nerve insulator and helps in the transmission of nerve signals. [NIH]

Muscle Fibers: Large single cells, either cylindrical or prismatic in shape, that form the basic unit of muscle tissue. They consist of a soft contractile substance enclosed in a tubular sheath. [NIH]

Muscular Atrophy: Derangement in size and number of muscle fibers occurring with aging, reduction in blood supply, or following immobilization, prolonged weightlessness, malnutrition, and particularly in denervation. [NIH]

Muscular Dystrophies: A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

Musculoskeletal Abnormalities: Congenital structural abnormalities and deformities of the musculoskeletal system. [NIH]

Musculoskeletal System: Themuscles, bones, and cartilage of the body. [NIH]

Mutagenesis: Process of generating genetic mutations. It may occur spontaneously or be induced by mutagens. [NIH]

Mutagens: Chemical agents that increase the rate of genetic mutation by interfering with the function of nucleic acids. A clastogen is a specific mutagen that causes breaks in chromosomes. [NIH]

Mydriatic: 1. Dilating the pupil. 2. Any drug that dilates the pupil. [EU]

Myelin: The fatty substance that covers and protects nerves. [NIH]

Myelodysplastic syndrome: Disease in which the bone marrow does not function normally. Also called preleukemia or smoldering leukemia. [NIH]

Myelography: X-ray visualization of the spinal cord following injection of contrast medium into the spinal arachnoid space. [NIH]

Myeloma: Cancer that arises in plasma cells, a type of white blood cell. [NIH]

Myocardial infarction: Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Myocardial Ischemia: A disorder of cardiac function caused by insufficient blood flow to the muscle tissue of the heart. The decreased blood flow may be due to narrowing of the coronary arteries (coronary arteriosclerosis), to obstruction by a thrombus (coronary thrombosis), or less commonly, to diffuse narrowing of arterioles and other small vessels within the heart. Severe interruption of the blood supply to the myocardial tissue may result in necrosis of cardiac muscle (myocardial infarction). [NIH]

Myocardial Reperfusion: Generally, restoration of blood supply to heart tissue which is ischemic due to decrease in normal blood supply. The decrease may result from any source including atherosclerotic obstruction, narrowing of the artery, or surgical clamping. Reperfusion can be induced to treat ischemia. Methods include chemical dissolution of an occluding thrombus, administration of vasodilator drugs, angioplasty, catheterization, and

artery bypass graft surgery. However, it is thought that reperfusion can itself further damage the ischemic tissue, causing myocardial reperfusion injury. [NIH]

Myocardial Reperfusion Injury: Functional, metabolic, or structural changes in ischemic heart muscle thought to result from reperfusion to the ischemic areas. Changes can be fatal to muscle cells and may include edema with explosive cell swelling and disintegration, sarcolemma disruption, fragmentation of mitochondria, contraction band necrosis, enzyme washout, and calcium overload. Other damage may include hemorrhage and ventricular arrhythmias. One possible mechanism of damage is thought to be oxygen free radicals. Treatment currently includes the introduction of scavengers of oxygen free radicals, and injury is thought to be prevented by warm blood cardioplegic infusion prior to reperfusion. [NIH]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myotonic Dystrophy: A condition presenting muscle weakness and wasting which may be progressive. [NIH]

Narcolepsy: A condition of unknown cause characterized by a periodic uncontrollable tendency to fall asleep. [NIH]

Narcosis: A general and nonspecific reversible depression of neuronal excitability, produced by a number of physical and chemical aspects, usually resulting in stupor. [NIH]

Narcotic: 1. Pertaining to or producing narcosis. 2. An agent that produces insensibility or stupor, applied especially to the opioids, i.e. to any natural or synthetic drug that has morphine-like actions. [EU]

Natriuresis: The excretion of abnormal amounts of sodium in the urine. [EU]

Nausea: An unpleasant sensation in the stomach usually accompanied by the urge to vomit. Common causes are early pregnancy, sea and motion sickness, emotional stress, intense pain, food poisoning, and various enteroviruses. [NIH]

NCI: National Cancer Institute. NCI, part of the National Institutes of Health of the United States Department of Health and Human Services, is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at http://cancer.gov. [NIH]

Nebramycin: A complex of antibiotic substances produced by Streptomyces tenebrarius. [NIH]

Neck Injuries: General or unspecified injuries to the neck. It includes injuries to the skin, muscles, and other soft tissues of the neck. [NIH]

Necrosis: A pathological process caused by the progressive degradative action of enzymes that is generally associated with severe cellular trauma. It is characterized by mitochondrial swelling, nuclear flocculation, uncontrolled cell lysis, and ultimately cell death. [NIH]

Need: A state of tension or dissatisfaction felt by an individual that impels him to action toward a goal he believes will satisfy the impulse. [NIH]

Nelfinavir: A potent HIV protease inhibitor. It is used in combination with other antiviral drugs in the treatment of HIV in both adults and children. [NIH]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

Neoplasms: New abnormal growth of tissue. Malignant neoplasms show a greater degree of anaplasia and have the properties of invasion and metastasis, compared to benign neoplasms. [NIH]

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining

to neoplasia (= the formation of a neoplasm). [EU]

Nephrectomy: Surgery to remove a kidney. Radical nephrectomy removes the kidney, the adrenal gland, nearby lymph nodes, and other surrounding tissue. Simple nephrectomy removes only the kidney. Partial nephrectomy removes the tumor but not the entire kidney. [NIH]

Nephritis: Inflammation of the kidney; a focal or diffuse proliferative or destructive process which may involve the glomerulus, tubule, or interstitial renal tissue. [EU]

Nephrolithiasis: Kidney stones. [NIH]

Nephrologist: A doctor who treats patients with kidney problems or hypertension. [NIH]

Nephrology: A subspecialty of internal medicine concerned with the anatomy, physiology, and pathology of the kidney. [NIH]

Nephron: A tiny part of the kidneys. Each kidney is made up of about 1 million nephrons, which are the working units of the kidneys, removing wastes and extra fluids from the blood. [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]

Nephrotoxic: Toxic or destructive to kidney cells. [EU]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

Nervous System: The entire nerve apparatus composed of the brain, spinal cord, nerves and ganglia. [NIH]

Networks: Pertaining to a nerve or to the nerves, a meshlike structure of interlocking fibers or strands. [NIH]

Neural: 1. Pertaining to a nerve or to the nerves. 2. Situated in the region of the spinal axis, as the neutral arch. [EU]

Neural 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]

Neurodegenerative Diseases: Hereditary and sporadic conditions which are characterized by progressive nervous system dysfunction. These disorders are often associated with atrophy of the affected central or peripheral nervous system structures. [NIH]

Neurogenic: Loss of bladder control caused by damage to the nerves controlling the bladder. [NIH]

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]

Neuropsychology: A branch of psychology which investigates the correlation between experience or behavior and the basic neurophysiological processes. The term neuropsychology stresses the dominant role of the nervous system. It is a more narrowly defined field than physiological psychology or psychophysiology. [NIH]

Neutralization: An act or process of neutralizing. [EU]

Neutrophil: A type of white blood cell. [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]

Nitrogen Dioxide: Nitrogen oxide (NO2). A highly poisonous gas. Exposure produces inflammation of lungs that may only cause slight pain or pass unnoticed, but resulting edema several days later may cause death. (From Merck, 11th ed) It is a major atmospheric pollutant that is able to absorb UV light that does not reach the earth's surface. [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]

Notochord: The rod-shaped body, composed of cells derived from the mesoblast and defining the primitive axis of the embryo. In lower vertebrates, it persists throughout life as the main axial support of the body, but in higher vertebrates it is replaced by the vertebral column. [NIH]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

Nucleic Acid Hybridization: The process whereby two single-stranded polynucleotides form a double-stranded molecule, with hydrogen bonding between the complementary bases in the two strains. [NIH]

Nucleic Acid Probes: Nucleic acid which complements a specific mRNA or DNA molecule, or fragment thereof; used for hybridization studies in order to identify microorganisms and for genetic studies. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nursing Care: Care given to patients by nursing service personnel. [NIH]

Nutrition Assessment: Evaluation and measurement of nutritional variables in order to assess the level of nutrition or the nutritional status of the individual. Nutrition surveys may be used in making the assessment. [NIH]

Nutritional Status: State of the body in relation to the consumption and utilization of nutrients. [NIH]

Observational study: An epidemiologic study that does not involve any intervention, experimental or otherwise. Such a study may be one in which nature is allowed to take its course, with changes in one characteristic being studied in relation to changes in other characteristics. Analytical epidemiologic methods, such as case-control and cohort study designs, are properly called observational epidemiology because the investigator is observing without intervention other than to record, classify, count, and statistically analyze results. [NIH]

Oliguria: Clinical manifestation of the urinary system consisting of a decrease in the amount of urine secreted. [NIH]

Oncogene: A gene that normally directs cell growth. If altered, an oncogene can promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by an environmental exposure to carcinogens. [NIH]

Oncogenic: Chemical, viral, radioactive or other agent that causes cancer; carcinogenic. [NIH]

Oncogenic Viruses: Viruses that produce tumors. [NIH]

Oocytes: Female germ cells in stages between the prophase of the first maturation division and the completion of the second maturation division. [NIH]

Operon: The genetic unit consisting of a feedback system under the control of an operator gene, in which a structural gene transcribes its message in the form of mRNA upon blockade of a repressor produced by a regulator gene. Included here is the attenuator site of bacterial operons where transcription termination is regulated. [NIH]

Ophthalmologic: Pertaining to ophthalmology (= the branch of medicine dealing with the eye). [EU]

Ophthalmology: A surgical specialty concerned with the structure and function of the eye and the medical and surgical treatment of its defects and diseases. [NIH]

Optic Disk: The portion of the optic nerve seen in the fundus with the ophthalmoscope. It is formed by the meeting of all the retinal ganglion cell axons as they enter the optic nerve. [NIH]

Orbital: Pertaining to the orbit (= the bony cavity that contains the eyeball). [EU]

Organ Culture: The growth in aseptic culture of plant organs such as roots or shoots, beginning with organ primordia or segments and maintaining the characteristics of the organ. [NIH]

Organ Transplantation: Transference of an organ between individuals of the same species or between individuals of different species. [NIH]

Organelles: Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum; lysomomes; plastids; and vacuoles. [NIH]

Osmolality: The concentration of osmotically active particles in solution expressed in terms of osmoles of solute per kilogram of solvent. The osmolality is directly proportional to the colligative properties of solutions; osmotic pressure, boiling point elevation, freezing point depression, and vapour pressure lowering. [EU]

Osmoles: The standard unit of osmotic pressure. [NIH]

Osmosis: Tendency of fluids (e.g., water) to move from the less concentrated to the more concentrated side of a semipermeable membrane. [NIH]

Osmotic: Pertaining to or of the nature of osmosis (= the passage of pure solvent from a solution of lesser to one of greater solute concentration when the two solutions are separated by a membrane which selectively prevents the passage of solute molecules, but is permeable to the solvent). [EU]

Osteoarthritis: A progressive, degenerative joint disease, the most common form of arthritis, especially in older persons. The disease is thought to result not from the aging process but from biochemical changes and biomechanical stresses affecting articular cartilage. In the foreign literature it is often called osteoarthrosis deformans. [NIH]

Osteodystrophy: Defective bone formation. [EU]

Osteoporosis: Reduction of bone mass without alteration in the composition of bone, leading to fractures. Primary osteoporosis can be of two major types: postmenopausal osteoporosis and age-related (or senile) osteoporosis. [NIH]

Ototoxic: Having a deleterious effect upon the eighth nerve, or upon the organs of hearing and balance. [EU]

Outpatient: A patient who is not an inmate of a hospital but receives diagnosis or treatment in a clinic or dispensary connected with the hospital. [NIH]

Ovarian Cysts: General term for cysts and cystic diseases of the ovary. [NIH]

Ovary: Either of the paired glands in the female that produce the female germ cells and secrete some of the female sex hormones. [NIH]

Overexpress: An excess of a particular protein on the surface of a cell. [NIH]

Ovum: A female germ cell extruded from the ovary at ovulation. [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]

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]

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]

Pancreas Transplant: A surgical procedure that involves replacing the pancreas of a person who has diabetes with a healthy pancreas that can make insulin. The healthy pancreas comes from a donor who has just died or from a living relative. A person can donate half a pancreas and still live normally. [NIH]

Pancreatic: Having to do with the pancreas. [NIH]

Pancreatic cancer: Cancer of the pancreas, a salivary gland of the abdomen. [NIH]

Pancreatic Ducts: Ducts that collect pancreatic juice from the pancreas and supply it to the duodenum. [NIH]

Pancreatic Juice: The fluid containing digestive enzymes secreted by the pancreas in response to food in the duodenum. [NIH]

Pancreatitis: Acute or chronic inflammation of the pancreas, which may be asymptomatic or symptomatic, and which is due to autodigestion of a pancreatic tissue by its own enzymes. It is caused most often by alcoholism or biliary tract disease; less commonly it may be associated with hyperlipaemia, hyperparathyroidism, abdominal trauma (accidental or operative injury), vasculitis, or uraemia. [EU]

Papilla: A small nipple-shaped elevation. [NIH]

Papillary: Pertaining to or resembling papilla, or nipple. [EU]

Papovaviridae: A family of small, non-enveloped DNA viruses affecting mostly mammals. Most members can induce tumors in hosts. There are two genera: Papillomavirus and Polyomavirus. [NIH]

Paralysis: Loss of ability to move all or part of the body. [NIH]

Parasite: An animal or a plant that lives on or in an organism of another species and gets at least some of its nutrition from that other organism. [NIH]

Parasitic: Having to do with or being a parasite. A parasite is an animal or a plant that lives on or in an organism of another species and gets at least some of its nutrients from it. [NIH]

Parenchyma: The essential elements of an organ; used in anatomical nomenclature as a general term to designate the functional elements of an organ, as distinguished from its framework, or stroma. [EU]

Parotid: The space that contains the parotid gland, the facial nerve, the external carotid artery, and the retromandibular vein. [NIH]

Paroxysmal: Recurring in paroxysms (= spasms or seizures). [EU]

Partial remission: The shrinking, but not complete disappearance, of a tumor in response to therapy. Also called partial response. [NIH]

Particle: A tiny mass of material. [EU]

Pathogenesis: The cellular events and reactions that occur in the development of disease. [NIH]

Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

Pathophysiology: Altered functions in an individual or an organ due to disease. [NIH]

Patient Care Management: Generating, planning, organizing, and administering medical and nursing care and services for patients. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

Pedigree: A record of one's ancestors, offspring, siblings, and their offspring that may be used to determine the pattern of certain genes or disease inheritance within a family. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Penicillamine: 3-Mercapto-D-valine. The most characteristic degradation product of the

penicillin antibiotics. It is used as an antirheumatic and as a chelating agent in Wilson's disease. [NIH]

Penicillin: An antibiotic drug used to treat infection. [NIH]

Penis: The external reproductive organ of males. It is composed of a mass of erectile tissue enclosed in three cylindrical fibrous compartments. Two of the three compartments, the corpus cavernosa, are placed side-by-side along the upper part of the organ. The third compartment below, the corpus spongiosum, houses the urethra. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Peptide T: N-(N-(N(2)-(N-(N-(N-(N-D-Alanyl L-seryl)-L-threonyl)-L-threonyl) L-threonyl)-L-asparaginyl)-L-tyrosyl) L-threonine. Octapeptide sharing sequence homology with HIV envelope protein gp120. It is potentially useful as antiviral agent in AIDS therapy. The core pentapeptide sequence, TTNYT, consisting of amino acids 4-8 in peptide T, is the HIV envelope sequence required for attachment to the CD4 receptor. [NIH]

Perfusion: Bathing an organ or tissue with a fluid. In regional perfusion, a specific area of the body (usually an arm or a leg) receives high doses of anticancer drugs through a blood vessel. Such a procedure is performed to treat cancer that has not spread. [NIH]

Pericardium: The fibroserous sac surrounding the heart and the roots of the great vessels. [NIH]

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]

Peripheral blood: Blood circulating throughout the body. [NIH]

Peripheral Nerves: The nerves outside of the brain and spinal cord, including the autonomic, cranial, and spinal nerves. Peripheral nerves contain non-neuronal cells and connective tissue as well as axons. The connective tissue layers include, from the outside to the inside, the epineurium, the perineurium, and the endoneurium. [NIH]

Peripheral Nervous System: The nervous system outside of the brain and spinal cord. The peripheral nervous system has autonomic and somatic divisions. The autonomic nervous system includes the enteric, parasympathetic, and sympathetic subdivisions. The somatic nervous system includes the cranial and spinal nerves and their ganglia and the peripheral sensory receptors. [NIH]

Peripheral Vascular Disease: Disease in the large blood vessels of the arms, legs, and feet. People who have had diabetes for a long time may get this because major blood vessels in their arms, legs, and feet are blocked and these limbs do not receive enough blood. The signs of PVD are aching pains in the arms, legs, and feet (especially when walking) and foot sores that heal slowly. Although people with diabetes cannot always avoid PVD, doctors say they have a better chance of avoiding it if they take good care of their feet, do not smoke, and keep both their blood pressure and diabetes under good control. [NIH]

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]

Peritoneal Dialysis, Continuous Ambulatory: Portable peritoneal dialysis using the

continuous (24 hours a day, 7 days a week) presence of peritoneal dialysis solution in the peritoneal cavity except for periods of drainage and instillation of fresh solution. [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]

Petechiae: Pinpoint, unraised, round red spots under the skin caused by bleeding. [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]

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]

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]

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]

Phenylalanine: An aromatic amino acid that is essential in the animal diet. It is a precursor of melanin, dopamine, noradrenalin, and thyroxine. [NIH]

Phospholipases: A class of enzymes that catalyze the hydrolysis of phosphoglycerides or glycerophosphatidates. EC 3.1.-. [NIH]

Phospholipids: Lipids containing one or more phosphate groups, particularly those derived from either glycerol (phosphoglycerides; glycerophospholipids) or sphingosine (sphingolipids). They are polar lipids that are of great importance for the structure and function of cell membranes and are the most abundant of membrane lipids, although not stored in large amounts in the system. [NIH]

Phosphorous: Having to do with or containing the element phosphorus. [NIH]

Phosphorus: A non-metallic element that is found in the blood, muscles, nevers, bones, and teeth, and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells.) [NIH]

Phosphorylation: The introduction of a phosphoryl group into a compound through the formation of an ester bond between the compound and a phosphorus moiety. [NIH]

Physical Examination: Systematic and thorough inspection of the patient for physical signs of disease or abnormality. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Physiology: The science that deals with the life processes and functions of organismus, their cells, tissues, and organs. [NIH]

Pigment: A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes, and hair. [NIH]

Pilot study: The initial study examining a new method or treatment. [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]

Plastids: Self-replicating cytoplasmic organelles of plant and algal cells that contain pigments and may synthesize and accumulate various substances. Plastids are used in phylogenetic studies. [NIH]

Platelet Activation: A series of progressive, overlapping events triggered by exposure of the platelets to subendothelial tissue. These events include shape change, adhesiveness, aggregation, and release reactions. When carried through to completion, these events lead to the formation of a stable hemostatic plug. [NIH]

Platelet Aggregation: The attachment of platelets to one another. This clumping together can be induced by a number of agents (e.g., thrombin, collagen) and is part of the mechanism leading to the formation of a thrombus. [NIH]

Platelet Transfusion: The transfer of blood platelets from a donor to a recipient or reinfusion to the donor. [NIH]

Platelets: A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called thrombocytes. [NIH]

Platinum: Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

Poisoning: A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

Polyarteritis Nodosa: A form of necrotizing vasculitis involving small- and medium-sized arteries. The signs and symptoms result from infarction and scarring of the affected organ system. [NIH]

Polycystic: An inherited disorder characterized by many grape-like clusters of fluid-filled cysts that make both kidneys larger over time. These cysts take over and destroy working kidney tissue. PKD may cause chronic renal failure and end-stage renal disease. [NIH]

Polycystic Kidney Diseases: Diseases that are characterized by the progressive expansion of a large number of tightly packed cysts within the kidney. [NIH]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand as a template. The polymerase copies the template in the 5'-3'direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

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]

Polyomavirus: A genus of the family papovaviridae consisting of potentially oncogenic viruses normally present in the host as a latent infection. The virus is oncogenic in hosts different from the species of origin. [NIH]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Polyuria: Urination of a large volume of urine with an increase in urinary frequency, commonly seen in diabetes. [NIH]

Popliteal: Compression of the nerve at the neck of the fibula. [NIH]

Portal Vein: A short thick vein formed by union of the superior mesenteric vein and the splenic vein. [NIH]

Posterior: Situated in back of, or in the back part of, or affecting the back or dorsal surface of the body. In lower animals, it refers to the caudal end of the body. [EU]

Postmenopausal: Refers to the time after menopause. Menopause is the time in a woman's life when menstrual periods stop permanently; also called "change of life." [NIH]

Postnatal: Occurring after birth, with reference to the newborn. [EU]

Postoperative: After surgery. [NIH]

Postoperative Complications: Pathologic processes that affect patients after a surgical procedure. They may or may not be related to the disease for which the surgery was done, and they may or may not be direct results of the surgery. [NIH]

Postsynaptic: Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

Post-translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Potassium: An element that is in the alkali group of metals. It has an atomic symbol K, atomic number 19, and atomic weight 39.10. It is the chief cation in the intracellular fluid of muscle and other cells. Potassium ion is a strong electrolyte and it plays a significant role in the regulation of fluid volume and maintenance of the water-electrolyte balance. [NIH]

Potassium Channels: Cell membrane glycoproteins selective for potassium ions. [NIH]

Potentiates: A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [NIH]

Potentiation: An overall effect of two drugs taken together which is greater than the sum of the effects of each drug taken alone. [NIH]

Practicability: A non-standard characteristic of an analytical procedure. It is dependent on the scope of the method and is determined by requirements such as sample throughout and costs. [NIH]

Practice Guidelines: Directions or principles presenting current or future rules of policy for the health care practitioner to assist him in patient care decisions regarding diagnosis, therapy, or related clinical circumstances. The guidelines may be developed by government agencies at any level, institutions, professional societies, governing boards, or by the convening of expert panels. The guidelines form a basis for the evaluation of all aspects of

health care and delivery. [NIH]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

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]

Preeclampsia: A toxaemia of late pregnancy characterized by hypertension, edema, and proteinuria, when convulsions and coma are associated, it is called eclampsia. [EU]

Preleukemia: Conditions in which the abnormalities in the peripheral blood or bone marrow represent the early manifestations of acute leukemia, but in which the changes are not of sufficient magnitude or specificity to permit a diagnosis of acute leukemia by the usual clinical criteria. [NIH]

Premenstrual: Occurring before menstruation. [EU]

Premenstrual Syndrome: A syndrome occurring most often during the last week of the menstrual cycle and ending soon after the onset of menses. Some of the symptoms are emotional instability, insomnia, headache, nausea, vomiting, abdominal distension, and painful breasts. [NIH]

Prenatal: Existing or occurring before birth, with reference to the fetus. [EU]

Prenatal Care: Care provided the pregnant woman in order to prevent complications, and decrease the incidence of maternal and prenatal mortality. [NIH]

Presynaptic: Situated proximal to a synapse, or occurring before the synapse is crossed. [EU]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Priapism: Persistent abnormal erection of the penis, usually without sexual desire, and accompanied by pain and tenderness. It is seen in diseases and injuries of the spinal cord, and may be caused by vesical calculus and certain injuries to the penis. [EU]

Primary endpoint: The main result that is measured at the end of a study to see if a given treatment worked (e.g., the number of deaths or the difference in survival between the treatment group and the control group). What the primary endpoint will be is decided before the study begins. [NIH]

Probe: An instrument used in exploring cavities, or in the detection and dilatation of strictures, or in demonstrating the potency of channels; an elongated instrument for exploring or sounding body cavities. [NIH]

Prodrug: A substance that gives rise to a pharmacologically active metabolite, although not itself active (i. e. an inactive precursor). [NIH]

Progeny: The offspring produced in any generation. [NIH]

Progesterone: Pregn-4-ene-3,20-dione. The principal progestational hormone of the body, secreted by the corpus luteum, adrenal cortex, and placenta. Its chief function is to prepare the uterus for the reception and development of the fertilized ovum. It acts as an

antiovulatory agent when administered on days 5-25 of the menstrual cycle. [NIH]

Progression: Increase in the size of a tumor or spread of cancer in the body. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Progressive disease: Cancer that is increasing in scope or severity. [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]

Pronephros: The primordial kidney; an excretory structure or its rudiments developing in the embryo before the mesonephros. [NIH]

Prophase: The first phase of cell division, in which the chromosomes become visible, the nucleus starts to lose its identity, the spindle appears, and the centrioles migrate toward opposite poles. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Proportional: Being in proportion : corresponding in size, degree, or intensity, having the same or a constant ratio; of, relating to, or used in determining proportions. [EU]

Prospective study: An epidemiologic study in which a group of individuals (a cohort), all free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

Prostaglandin: Any of a group of components derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway that are extremely potent mediators of a diverse group of physiologic processes. The abbreviation for prostaglandin is PG; specific compounds are designated by adding one of the letters A through I to indicate the type of substituents found on the hydrocarbon skeleton and a subscript (1, 2 or 3) to indicate the number of double bonds in the hydrocarbon skeleton e.g., PGE2. The predominant naturally occurring prostaglandins all have two double bonds and are synthesized from arachidonic acid (5,8,11,14-eicosatetraenoic acid) by the pathway shown in the illustration. The 1 series and 3 series are produced by the same pathway with fatty acids having one fewer double bond (8,11,14-eicosatrienoic acid or one more double bond (5,8,11,14,17-eicosapentaenoic acid) than arachidonic acid. The subscript a or ß indicates the configuration at C-9 (a denotes a substituent below the plane of the ring, ß, above the plane). The naturally occurring PGF's have the a configuration, e.g., PGF2a. All of the prostaglandins act by binding to specific cell-surface receptors causing an increase in the level of the intracellular second messenger cyclic AMP (and in some cases cyclic GMP also). The effect produced by the cyclic AMP increase depends on the specific cell type. In some cases there is also a positive feedback effect. Increased cyclic AMP increases prostaglandin synthesis leading to further increases in cyclic AMP. [EU]

Prostaglandins A: (13E,15S)-15-Hydroxy-9-oxoprosta-10,13-dien-1-oic acid (PGA(1)); (5Z,13E,15S)-15-hydroxy-9-oxoprosta-5,10,13-trien-1-oic acid (PGA(2)); (5Z,13E,15S,17Z)-15-hydroxy-9-oxoprosta-5,10,13,17-tetraen-1-oic acid (PGA(3)). A group of naturally occurring secondary prostaglandins derived from PGE. PGA(1) and PGA(2) as well as their 19-hydroxy derivatives are found in many organs and tissues. [NIH]

Prostaglandins E: (11 alpha,13E,15S)-11,15-Dihydroxy-9-oxoprost-13-en-1-oic acid (PGE(1)); (5Z,11 alpha,13E,15S)-11,15-dihydroxy-9-oxoprosta-5,13-dien-1-oic acid (PGE(2)); and (5Z,11 alpha,13E,15S,17Z)-11,15-dihydroxy-9-oxoprosta-5,13,17-trien-1-oic acid (PGE(3)). Three of

the six naturally occurring prostaglandins. They are considered primary in that no one is derived from another in living organisms. Originally isolated from sheep seminal fluid and vesicles, they are found in many organs and tissues and play a major role in mediating various physiological activities. [NIH]

Prostate: A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

Protease Inhibitors: Compounds which inhibit or antagonize biosynthesis or actions of proteases (endopeptidases). [NIH]

Protective Agents: Synthetic or natural substances which are given to prevent a disease or disorder or are used in the process of treating a disease or injury due to a poisonous agent. [NIH]

Protein C: A vitamin-K dependent zymogen present in the blood, which, upon activation by thrombin and thrombomodulin exerts anticoagulant properties by inactivating factors Va and VIIIa at the rate-limiting steps of thrombin formation. [NIH]

Protein Conformation: The characteristic 3-dimensional shape of a protein, including the secondary, supersecondary (motifs), tertiary (domains) and quaternary structure of the peptide chain. Quaternary protein structure describes the conformation assumed by multimeric proteins (aggregates of more than one polypeptide chain). [NIH]

Protein Kinases: A family of enzymes that catalyze the conversion of ATP and a protein to ADP and a phosphoprotein. EC 2.7.1.37. [NIH]

Protein S: The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

Protein Subunits: Single chains of amino acids that are the units of a multimeric protein. They can be identical or non-identical subunits. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

Proteinuria: The presence of protein in the urine, indicating that the kidneys are not working properly. [NIH]

Proteoglycan: A molecule that contains both protein and glycosaminoglycans, which are a type of polysaccharide. Proteoglycans are found in cartilage and other connective tissues. [NIH]

Proteolytic: 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Protocol: The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other aspects of trial design. [NIH]

Protons: Stable elementary particles having the smallest known positive charge, found in the nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

Protozoa: A subkingdom consisting of unicellular organisms that are the simplest in the animal kingdom. Most are free living. They range in size from submicroscopic to

macroscopic. Protozoa are divided into seven phyla: Sarcomastigophora, Labyrinthomorpha, Apicomplexa, Microspora, Ascetospora, Myxozoa, and Ciliophora. [NIH]

Proximal: Nearest; closer to any point of reference; opposed to distal. [EU]

Pseudogenes: Genes bearing close resemblance to known genes at different loci, but rendered non-functional by additions or deletions in structure that prevent normal transcription or translation. When lacking introns and containing a poly-A segment near the downstream end (as a result of reverse copying from processed nuclear RNA into double-stranded DNA), they are called processed genes. [NIH]

Psoriasis: A common genetically determined, chronic, inflammatory skin disease characterized by rounded erythematous, dry, scaling patches. The lesions have a predilection for nails, scalp, genitalia, extensor surfaces, and the lumbosacral region. Accelerated epidermopoiesis is considered to be the fundamental pathologic feature in psoriasis. [NIH]

Psychiatry: The medical science that deals with the origin, diagnosis, prevention, and treatment of mental disorders. [NIH]

Psychic: Pertaining to the psyche or to the mind; mental. [EU]

Psychology: The science dealing with the study of mental processes and behavior in man and animals. [NIH]

Psychophysiology: The study of the physiological basis of human and animal behavior. [NIH]

Psychosis: A mental disorder characterized by gross impairment in reality testing as evidenced by delusions, hallucinations, markedly incoherent speech, or disorganized and agitated behaviour without apparent awareness on the part of the patient of the incomprehensibility of his behaviour; the term is also used in a more general sense to refer to mental disorders in which mental functioning is sufficiently impaired as to interfere grossly with the patient's capacity to meet the ordinary demands of life. Historically, the term has been applied to many conditions, e.g. manic-depressive psychosis, that were first described in psychotic patients, although many patients with the disorder are not judged psychotic. [EU]

Puberty: The period during which the secondary sex characteristics begin to develop and the capability of sexual reproduction is attained. [EU]

Public 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]

Pupil: The aperture in the iris through which light passes. [NIH]

Purines: A series of heterocyclic compounds that are variously substituted in nature and are

known also as purine bases. They include adenine and guanine, constituents of nucleic acids, as well as many alkaloids such as caffeine and theophylline. Uric acid is the metabolic end product of purine metabolism. [NIH]

Purpura: Purplish or brownish red discoloration, easily visible through the epidermis, caused by hemorrhage into the tissues. [NIH]

Pyelonephritis: Inflammation of the kidney and its pelvis, beginning in the interstitium and rapidly extending to involve the tubules, glomeruli, and blood vessels; due to bacterial infection. [EU]

Quality of Life: A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

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]

Radio Waves: That portion of the electromagnetic spectrum beyond the microwaves, with wavelengths as high as 30 KM. They are used in communications, including television. Short Wave or HF (high frequency), UHF (ultrahigh frequency) and VHF (very high frequency) waves are used in citizen's band communication. [NIH]

Radioactive: Giving off radiation. [NIH]

Radiography: Examination of any part of the body for diagnostic purposes by means of roentgen rays, recording the image on a sensitized surface (such as photographic film). [NIH]

Radioimmunoassay: Classic quantitative assay for detection of antigen-antibody reactions using a radioactively labeled substance (radioligand) either directly or indirectly to measure the binding of the unlabeled substance to a specific antibody or other receptor system. Non-immunogenic substances (e.g., haptens) can be measured if coupled to larger carrier proteins (e.g., bovine gamma-globulin or human serum albumin) capable of inducing antibody formation. [NIH]

Radiological: Pertaining to radiodiagnostic and radiotherapeutic procedures, and interventional radiology or other planning and guiding medical radiology. [NIH]

Radiology: A specialty concerned with the use of x-ray and other forms of radiant energy in the diagnosis and treatment of disease. [NIH]

Ramipril: A long-acting angiotensin-converting enzyme inhibitor. It is a prodrug that is transformed in the liver to its active metabolite ramiprilat. [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]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Reality Testing: The individual's objective evaluation of the external world and the ability

to differentiate adequately between it and the internal world; considered to be a primary ego function. [NIH]

Receptor: A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

Recombinant: A cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

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]

Red blood cells: RBCs. Cells that carry oxygen to all parts of the body. Also called erythrocytes. [NIH]

Red Nucleus: A pinkish-yellow portion of the midbrain situated in the rostral mesencephalic tegmentum. It receives a large projection from the contralateral half of the cerebellum via the superior cerebellar peduncle and a projection from the ipsilateral motor cortex. [NIH]

Reductase: Enzyme converting testosterone to dihydrotestosterone. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

Reflux: The term used when liquid backs up into the esophagus from the stomach. [NIH]

Refraction: A test to determine the best eyeglasses or contact lenses to correct a refractive error (myopia, hyperopia, or astigmatism). [NIH]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Regional Medical Programs: Coordination of activities and programs among health care institutions within defined geographic areas for the purpose of improving delivery and quality of medical care to the patients. These programs are mandated under U.S. Public Law 89-239. [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]

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 agenesis: The absence or severe malformation of one or both kidneys. [NIH]

Renal Artery: A branch of the abdominal aorta which supplies the kidneys, adrenal glands and ureters. [NIH]

Renal Circulation: The circulation of the blood through the vessels of the kidney. [NIH]

Renal cysts: Abnormal fluid-filled sacs in the kidney that range in size from microscopic to much larger. Many simple cysts are harmless, while other types can seriously damage the kidneys. [NIH]

Renal Dialysis: Removal of certain elements from the blood based on the difference in their rates of diffusion through a semipermeable membrane. [NIH]

Renal failure: Progressive renal insufficiency and uremia, due to irreversible and progressive renal glomerular tubular or interstitial disease. [NIH]

Renal Osteodystrophy: Decalcification of bone due to hyperparathyroidism secondary to chronic kidney disease. [NIH]

Renal pelvis: The area at the center of the kidney. Urine collects here and is funneled into the ureter, the tube that connects the kidney to the bladder. [NIH]

Renal Replacement Therapy: Procedures which temporarily or permanently remedy insufficient cleansing of body fluids by the kidneys. [NIH]

Renal tubular: A defect in the kidneys that hinders their normal excretion of acids. Failure to excrete acids can lead to weak bones, kidney stones, and poor growth in children. [NIH]

Renin: An enzyme which is secreted by the kidney and is formed from prorenin in plasma and kidney. The enzyme cleaves the Leu-Leu bond in angiotensinogen to generate angiotensin I. EC 3.4.23.15. (Formerly EC 3.4.99.19). [NIH]

Renin-Angiotensin System: A system consisting of renin, angiotensin-converting enzyme, and angiotensin II. Renin, an enzyme produced in the kidney, acts on angiotensinogen, an alpha-2 globulin produced by the liver, forming angiotensin I. The converting enzyme contained in the lung acts on angiotensin I in the plasma converting it to angiotensin II, the most powerful directly pressor substance known. It causes contraction of the arteriolar smooth muscle and has other indirect actions mediated through the adrenal cortex. [NIH]

Reperfusion: Restoration of blood supply to tissue which is ischemic due to decrease in normal blood supply. The decrease may result from any source including atherosclerotic obstruction, narrowing of the artery, or surgical clamping. It is primarily a procedure for treating infarction or other ischemia, by enabling viable ischemic tissue to recover, thus limiting further necrosis. However, it is thought that reperfusion can itself further damage the ischemic tissue, causing reperfusion injury. [NIH]

Reperfusion Injury: Functional, metabolic, or structural changes, including necrosis, in ischemic tissues thought to result from reperfusion to ischemic areas of the tissue. The most common instance is myocardial reperfusion injury. [NIH]

Repressor: Any of the specific allosteric protein molecules, products of regulator genes, which bind to the operator of operons and prevent RNA polymerase from proceeding into the operon to transcribe messenger RNA. [NIH]

Resection: Removal of tissue or part or all of an organ by surgery. [NIH]

Resorption: The loss of substance through physiologic or pathologic means, such as loss of dentin and cementum of a tooth, or of the alveolar process of the mandible or maxilla. [EU]

Respiration: The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

Respiratory Physiology: Functions and activities of the respiratory tract as a whole or of any of its parts. [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]

Retinae: A congenital notch or cleft of the retina, usually located inferiorly. [NIH]

Retinal: 1. Pertaining to the retina. 2. The aldehyde of retinol, derived by the oxidative enzymatic splitting of absorbed dietary carotene, and having vitamin A activity. In the retina, retinal combines with opsins to form visual pigments. One isomer, 11-cis retinal

combines with opsin in the rods (scotopsin) to form rhodopsin, or visual purple. Another, all-trans retinal (trans-r.); visual yellow; xanthopsin) results from the bleaching of rhodopsin by light, in which the 11-cis form is converted to the all-trans form. Retinal also combines with opsins in the cones (photopsins) to form the three pigments responsible for colour vision. Called also retinal, and retinene1. [EU]

Retinoblastoma: An eye cancer that most often occurs in children younger than 5 years. It occurs in hereditary and nonhereditary (sporadic) forms. [NIH]

Retinoids: Derivatives of vitamin A. Used clinically in the treatment of severe cystic acne, psoriasis, and other disorders of keratinization. Their possible use in the prophylaxis and treatment of cancer is being actively explored. [NIH]

Retinol: Vitamin A. It is essential for proper vision and healthy skin and mucous membranes. Retinol is being studied for cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Retinopathy: 1. Retinitis (= inflammation of the retina). 2. Retinosis (= degenerative, noninflammatory condition of the retina). [EU]

Retrovirus: A member of a group of RNA viruses, the RNA of which is copied during viral replication into DNA by reverse transcriptase. The viral DNA is then able to be integrated into the host chromosomal DNA. [NIH]

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]

Rhinorrhea: The free discharge of a thin nasal mucus. [EU]

Ribavirin: 1-beta-D-Ribofuranosyl-1H-1,2,4-triazole-3-carboxamide. A nucleoside antimetabolite antiviral agent that blocks nucleic acid synthesis and is used against both RNA and DNA viruses. [NIH]

Ribose: A pentose active in biological systems usually in its D-form. [NIH]

Ribosome: A granule of protein and RNA, synthesized in the nucleolus and found in the cytoplasm of cells. Ribosomes are the main sites of protein synthesis. Messenger RNA attaches to them and there receives molecules of transfer RNA bearing amino acids. [NIH]

Rickettsiae: One of a group of obligate intracellular parasitic microorganisms, once regarded as intermediate in their properties between bacteria and viruses but now classified as bacteria in the order Rickettsiales, which includes 17 genera and 3 families: Rickettsiace. [NIH]

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]

Rod: A reception for vision, located in the retina. [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]

Saquinavir: An HIV protease inhibitor which acts as an analog of an HIV protease cleavage site. It is a highly specific inhibitor of HIV-1 and HIV-2 proteases. [NIH]

Sarcoidosis: An idiopathic systemic inflammatory granulomatous disorder comprised of epithelioid and multinucleated giant cells with little necrosis. It usually invades the lungs with fibrosis and may also involve lymph nodes, skin, liver, spleen, eyes, phalangeal bones, and parotid glands. [NIH]

Satellite: Applied to a vein which closely accompanies an artery for some distance; in cytogenetics, a chromosomal agent separated by a secondary constriction from the main body of the chromosome. [NIH]

Scalpel: A small pointed knife with a convex edge. [NIH]

Scatter: The extent to which relative success and failure are divergently manifested in qualitatively different tests. [NIH]

Schizoid: Having qualities resembling those found in greater degree in schizophrenics; a person of schizoid personality. [NIH]

Schizophrenia: A mental disorder characterized by a special type of disintegration of the personality. [NIH]

Schizotypal Personality Disorder: A personality disorder in which there are oddities of thought (magical thinking, paranoid ideation, suspiciousness), perception (illusions, depersonalization), speech (digressive, vague, overelaborate), and behavior (inappropriate affect in social interactions, frequently social isolation) that are not severe enough to characterize schizophrenia. [NIH]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Sebaceous: Gland that secretes sebum. [NIH]

Sebaceous gland: Gland that secretes sebum. [NIH]

Sebum: The oily substance secreted by sebaceous glands. It is composed of keratin, fat, and cellular debris. [NIH]

Secretion: 1. The process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. Any substance produced by secretion. [EU]

Secretory: Secreting; relating to or influencing secretion or the secretions. [NIH]

Sediment: A precipitate, especially one that is formed spontaneously. [EU]

Segmental: Describing or pertaining to a structure which is repeated in similar form in successive segments of an organism, or which is undergoing segmentation. [NIH]

Segmentation: The process by which muscles in the intestines move food and wastes through the body. [NIH]

Segregation: The separation in meiotic cell division of homologous chromosome pairs and their contained allelomorphic gene pairs. [NIH]

Seizures: Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena. Recurrent seizures are usually referred to as epilepsy or "seizure disorder." [NIH]

Self Care: Performance of activities or tasks traditionally performed by professional health care providers. The concept includes care of oneself or one's family and friends. [NIH]

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]

Seminal fluid: Fluid from the prostate and other sex glands that helps transport sperm out of the man's body during orgasm. Seminal fluid contains sugar as an energy source for sperm. [NIH]

Semisynthetic: Produced by chemical manipulation of naturally occurring substances. [EU]

Senile: Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

Sensibility: The ability to receive, feel and appreciate sensations and impressions; the quality of being sensitive; the extend to which a method gives results that are free from false negatives. [NIH]

Sepsis: The presence of bacteria in the bloodstream. [NIH]

Septic: Produced by or due to decomposition by microorganisms; putrefactive. [EU]

Septicemia: Systemic disease associated with the presence and persistence of pathogenic microorganisms or their toxins in the blood. Called also blood poisoning. [EU]

Sequence Analysis: A multistage process that includes the determination of a sequence (protein, carbohydrate, etc.), its fragmentation and analysis, and the interpretation of the resulting sequence information. [NIH]

Sequence Homology: The degree of similarity between sequences. Studies of amino acid and nucleotide sequences provide useful information about the genetic relatedness of certain species. [NIH]

Sequencing: The determination of the order of nucleotides in a DNA or RNA chain. [NIH]

Serine: A non-essential amino acid occurring in natural form as the L-isomer. It is synthesized from glycine or threonine. It is involved in the biosynthesis of purines, pyrimidines, and other amino acids. [NIH]

Serotonin: A biochemical messenger and regulator, synthesized from the essential amino acid L-tryptophan. In humans it is found primarily in the central nervous system, gastrointestinal tract, and blood platelets. Serotonin mediates several important physiological functions including neurotransmission, gastrointestinal motility, hemostasis, and cardiovascular integrity. Multiple receptor families (receptors, serotonin) explain the broad physiological actions and distribution of this biochemical mediator. [NIH]

Serous: Having to do with serum, the clear liquid part of blood. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

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]

Sex Determination: The biological characteristics which distinguish human beings as female or male. [NIH]

Shock: The general bodily disturbance following a severe injury; an emotional or moral upset occasioned by some disturbing or unexpected experience; disruption of the circulation, which can upset all body functions: sometimes referred to as circulatory shock. [NIH]

Side effect: A consequence other than the one(s) for which an agent or measure is used, as the adverse effects produced by a drug, especially on a tissue or organ system other than the one sought to be benefited by its administration. [EU]

Signal Transduction: The intercellular or intracellular transfer of information (biological activation/inhibition) through a signal pathway. In each signal transduction system, an activation/inhibition signal from a biologically active molecule (hormone, neurotransmitter) is mediated via the coupling of a receptor/enzyme to a second messenger system or to an ion channel. Signal transduction plays an important role in activating cellular functions, cell differentiation, and cell proliferation. Examples of signal transduction systems are the GABA-postsynaptic receptor-calcium ion channel system, the receptor-mediated T-cell activation pathway, and the receptor-mediated activation of phospholipases. Those coupled to membrane depolarization or intracellular release of calcium include the receptor-mediated activation of cytotoxic functions in granulocytes and the synaptic potentiation of protein kinase activation. Some signal transduction pathways may be part of larger signal transduction pathways; for example, protein kinase activation is part of the platelet activation signal pathway. [NIH]

Signs and Symptoms: Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [NIH]

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]

Skull: The skeleton of the head including the bones of the face and the bones enclosing the brain. [NIH]

Small intestine: The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

Smoldering leukemia: Disease in which the bone marrow does not function normally. Also called preleukemia or myelodysplastic syndrome. [NIH]

Smooth muscle: Muscle that performs automatic tasks, such as constricting blood vessels. [NIH]

Smooth Muscle Tumor: A tumor composed of smooth muscle tissue, as opposed to leiomyoma, a tumor derived from smooth muscle. [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 Work: The use of community resources, individual case work, or group work to

promote the adaptive capacities of individuals in relation to their social and economic environments. It includes social service agencies. [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]

Soma: The body as distinct from the mind; all the body tissue except the germ cells; all the axial body. [NIH]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Somatic mutations: Alterations in DNA that occur after conception. Somatic mutations can occur in any of the cells of the body except the germ cells (sperm and egg) and therefore are not passed on to children. These alterations can (but do not always) cause cancer or other diseases. [NIH]

Somites: Paired, segmented masses of mesodermal tissue that form along the length of the neural tube during the early stage of embryonic development. They give rise to the vertebral column and other tissues including voluntary muscle, bone, connective tissue, and the dermal layers of the skin. [NIH]

Sound wave: An alteration of properties of an elastic medium, such as pressure, particle displacement, or density, that propagates through the medium, or a superposition of such alterations. [NIH]

Soy Proteins: Proteins which are present in or isolated from soybeans. [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]

Spices: The dried seeds, bark, root, stems, buds, leaves, or fruit of aromatic plants used to season food. [NIH]

Spina bifida: A defect in development of the vertebral column in which there is a central deficiency of the vertebral lamina. [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]

Splenectomy: An operation to remove the spleen. [NIH]

Splenic Vein: Vein formed by the union (at the hilus of the spleen) of several small veins from the stomach, pancreas, spleen and mesentery. [NIH]

Splenomegaly: Enlargement of the spleen. [NIH]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [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]

Staphylococcus: A genus of gram-positive, facultatively anaerobic, coccoid bacteria. Its organisms occur singly, in pairs, and in tetrads and characteristically divide in more than one plane to form irregular clusters. Natural populations of Staphylococcus are membranes of warm-blooded animals. Some species are opportunistic pathogens of humans and animals. [NIH]

Stavudine: A dideoxynucleoside analog that inhibits reverse transcriptase and has in vitro activity against HIV. [NIH]

Stem Cells: Relatively undifferentiated cells of the same lineage (family type) that retain the ability to divide and cycle throughout postnatal life to provide cells that can become specialized and take the place of those that die or are lost. [NIH]

Sterility: 1. The inability to produce offspring, i.e., the inability to conceive (female s.) or to induce conception (male s.). 2. The state of being aseptic, or free from microorganisms. [EU]

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]

Steroid therapy: Treatment with corticosteroid drugs to reduce swelling, pain, and other symptoms of inflammation. [NIH]

Stimulant: 1. Producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. An agent or remedy that produces stimulation. [EU]

Stimulus: That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Stool: The waste matter discharged in a bowel movement; feces. [NIH]

Strand: DNA normally exists in the bacterial nucleus in a helix, in which two strands are coiled together. [NIH]

Stress: Forcibly exerted influence; pressure. Any condition or situation that causes strain or tension. Stress may be either physical or psychologic, or both. [NIH]

Striate: Recurrent branch of the anterior cerebral artery which supplies the anterior limb of the internal capsule. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Stroma: The middle, thickest layer of tissue in the cornea. [NIH]

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]

Strophanthins: A number of different cardioactive glycosides obtained from Strophanthus species. ouabain is from S. gratus and cymarine from S. kombe. They are used like the digitalis glycosides. [NIH]

Stupor: Partial or nearly complete unconsciousness, manifested by the subject's responding only to vigorous stimulation. Also, in psychiatry, a disorder marked by reduced responsiveness. [EU]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subarachnoid: Situated or occurring between the arachnoid and the pia mater. [EU]

Subclavian: The direct continuation of the axillary vein at the lateral border of the first rib. It passes medially to join the internal jugular vein and form the brachiocephalic vein on each side. [NIH]

Subclavian Artery: Artery arising from the brachiocephalic trunk on the right side and from the arch of the aorta on the left side. It distributes to the neck, thoracic wall, spinal cord, brain, meninges, and upper limb. [NIH]

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]

Submaxillary: Four to six lymph glands, located between the lower jaw and the submandibular salivary gland. [NIH]

Subspecies: A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

Substance P: An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

Suction: The removal of secretions, gas or fluid from hollow or tubular organs or cavities by means of a tube and a device that acts on negative pressure. [NIH]

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]

Support group: A group of people with similar disease who meet to discuss how better to cope with their cancer and treatment. [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]

Survival Rate: The proportion of survivors in a group, e.g., of patients, studied and followed over a period, or the proportion of persons in a specified group alive at the beginning of a time interval who survive to the end of the interval. It is often studied using life table methods. [NIH]

Sympathectomy: The removal or interruption of some part of the sympathetic nervous system for therapeutic or research purposes. [NIH]

Sympathetic Nervous System: The thoracolumbar division of the autonomic nervous system. Sympathetic preganglionic fibers originate in neurons of the intermediolateral column of the spinal cord and project to the paravertebral and prevertebral ganglia, which in turn project to target organs. The sympathetic nervous system mediates the body's response to stressful situations, i.e., the fight or flight reactions. It often acts reciprocally to the parasympathetic system. [NIH]

Sympathomimetic: 1. Mimicking the effects of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. 2. An agent that produces effects similar to those of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. Called also adrenergic. [EU]

Symphysis: A secondary cartilaginous joint. [NIH]

Symptomatic: Having to do with symptoms, which are signs of a condition or disease. [NIH]

Symptomatology: 1. That branch of medicine with treats of symptoms; the systematic discussion of symptoms. 2. The combined symptoms of a disease. [EU]

Synapsis: The pairing between homologous chromosomes of maternal and paternal origin during the prophase of meiosis, leading to the formation of gametes. [NIH]

Synaptic: Pertaining to or affecting a synapse (= site of functional apposition between neurons, at which an impulse is transmitted from one neuron to another by electrical or chemical means); pertaining to synapsis (= pairing off in point-for-point association of homologous chromosomes from the male and female pronuclei during the early prophase of meiosis). [EU]

Synaptic Transmission: The communication from a neuron to a target (neuron, muscle, or secretory cell) across a synapse. In chemical synaptic transmission, the presynaptic neuron releases a neurotransmitter that diffuses across the synaptic cleft and binds to specific synaptic receptors. These activated receptors modulate ion channels and/or second-messenger systems to influence the postsynaptic cell. Electrical transmission is less common in the nervous system, and, as in other tissues, is mediated by gap junctions. [NIH]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Synovial: Of pertaining to, or secreting synovia. [EU]

Systemic: Affecting the entire body. [NIH]

Systemic disease: Disease that affects the whole 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]

Systole: Period of contraction of the heart, especially of the ventricles. [NIH]

Systolic: Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

Systolic pressure: The highest pressure to which blood pressure rises with the contraction of the ventricles. [NIH]

Talin: A 235-kDa cytoplasmic protein that is also found in platelets. It has been localized to regions of cell-substrate adhesion. It binds to integrins, vinculin, and actins and appears to participate in generating a transmembrane connection between the extracellular matrix and the cytoskeleton. [NIH]

Taxanes: Anticancer drugs that inhibit cancer cell growth by stopping cell division. Also called antimitotic or antimicrotubule agents or mitotic inhibitors. [NIH]

Technetium: The first artificially produced element and a radioactive fission product of uranium. The stablest isotope has a mass number 99 and is used diagnostically as a radioactive imaging agent. Technetium has the atomic symbol Tc, atomic number 43, and atomic weight 98.91. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

Temporal: One of the two irregular bones forming part of the lateral surfaces and base of the skull, and containing the organs of hearing. [NIH]

Teratogens: An agent that causes the production of physical defects in the developing embryo. [NIH]

Terminator: A DNA sequence sited at the end of a transcriptional unit that signals the end of transcription. [NIH]

Tetracycline: An antibiotic originally produced by Streptomyces viridifaciens, but used mostly in synthetic form. It is an inhibitor of aminoacyl-tRNA binding during protein synthesis. [NIH]

Thalamic: Cell that reaches the lateral nucleus of amygdala. [NIH]

Thalamic Diseases: Disorders of the centrally located thalamus, which integrates a wide range of cortical and subcortical information. Manifestations include sensory loss, movement disorders; ataxia, pain syndromes, visual disorders, a variety of neuropsychological conditions, and coma. Relatively common etiologies include cerebrovascular disorders; craniocerebral trauma; brain neoplasms; brain hypoxia; intracranial hemorrhages; and infectious processes. [NIH]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thoracic: Having to do with the chest. [NIH]

Thorax: A part of the trunk between the neck and the abdomen; the chest. [NIH]

Threonine: An essential amino acid occurring naturally in the L-form, which is the active form. It is found in eggs, milk, gelatin, and other proteins. [NIH]

Threshold: For a specified sensory modality (e. g. light, sound, vibration), the lowest level (absolute threshold) or smallest difference (difference threshold, difference limen) or intensity of the stimulus discernible in prescribed conditions of stimulation. [NIH]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombocytes: Blood cells that help prevent bleeding by causing blood clots to form. Also called platelets. [NIH]

Thrombocytopenia: A decrease in the number of blood platelets. [NIH]

Thromboembolism: Obstruction of a vessel by a blood clot that has been transported from a distant site by the blood stream. [NIH]

Thrombomodulin: A cell surface glycoprotein of endothelial cells that binds thrombin and serves as a cofactor in the activation of protein C and its regulation of blood coagulation. [NIH]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thrombus: An aggregation of blood factors, primarily platelets and fibrin with entrapment of cellular elements, frequently causing vascular obstruction at the point of its formation. Some authorities thus differentiate thrombus formation from simple coagulation or clot formation. [EU]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [NIH]

Thyroxine: An amino acid of the thyroid gland which exerts a stimulating effect on thyroid metabolism. [NIH]

Tin: A trace element that is required in bone formation. It has the atomic symbol Sn, atomic number 50, and atomic weight 118.71. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Tissue Culture: Maintaining or growing of tissue, organ primordia, or the whole or part of an organ in vitro so as to preserve its architecture and/or function (Dorland, 28th ed). Tissue culture includes both organ culture and cell culture. [NIH]

Tobramycin: An aminoglycoside, broad-spectrum antibiotic produced by Streptomyces tenebrarius. It is effective against gram-negative bacteria, especially the Pseudomonas species. It is a 10% component of the antibiotic complex, nebramycin, produced by the same species. [NIH]

Tolerance: 1. The ability to endure unusually large doses of a drug or toxin. 2. Acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

Tomography: Imaging methods that result in sharp images of objects located on a chosen plane and blurred images located above or below the plane. [NIH]

Tonic: 1. Producing and restoring the normal tone. 2. Characterized by continuous tension. 3. A term formerly used for a class of medicinal preparations believed to have the power of restoring normal tone to tissue. [EU]

Tooth Abnormalities: Congenital absence of or defects in structures of the teeth. [NIH]

Topical: On the surface of the body. [NIH]

Torsion: A twisting or rotation of a bodily part or member on its axis. [NIH]

Toxaemia: 1. The condition resulting from the spread of bacterial products (toxins) by the bloodstream. 2. A condition resulting from metabolic disturbances, e.g. toxaemia of pregnancy. [EU]

Toxic: Having to do with poison or something harmful to the body. Toxic substances

usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

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]

Toxins: Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals. [NIH]

Trace element: Substance or element essential to plant or animal life, but present in extremely small amounts. [NIH]

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]

Transcutaneous: Transdermal. [EU]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

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]

Transforming Growth Factor alpha: Factor isolated in a variety of tissues including epithelium, and maternal decidua. It is closely related to epidermal growth factor and binds to the EGF receptor. TGF-alpha acts synergistically with TGF-beta in inducing phenotypic transformation, but its physiological role is unknown. [NIH]

Transforming Growth Factor beta: A factor synthesized in a wide variety of tissues. It acts synergistically with TGF-alpha in inducing phenotypic transformation and can also act as a negative autocrine growth factor. TGF-beta has a potential role in embryonal development, cellular differentiation, hormone secretion, and immune function. TGF-beta is found mostly as homodimer forms of separate gene products TGF-beta1, TGF-beta2 or TGF-beta3. Heterodimers composed of TGF-beta1 and 2 (TGF-beta1.2) or of TGF-beta2 and 3 (TGF-beta2.3) have been isolated. The TGF-beta proteins are synthesized as precursor proteins. [NIH]

Transfusion: The infusion of components of blood or whole blood into the bloodstream. The blood may be donated from another person, or it may have been taken from the person earlier and stored until needed. [NIH]

Translation: The process whereby the genetic information present in the linear sequence of ribonucleotides in mRNA is converted into a corresponding sequence of amino acids in a protein. It occurs on the ribosome and is unidirectional. [NIH]

Translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Translocation: The movement of material in solution inside the body of the plant. [NIH]

Transmitter: A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [NIH]

Transplantation: Transference of a tissue or organ, alive or dead, within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Transport Vesicles: Vesicles that are involved in shuttling cargo from the interior of the cell to the cell surface, from the cell surface to the interior, across the cell or around the cell to various locations. [NIH]

Trauma: Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [NIH]

Treatment Outcome: Evaluation undertaken to assess the results or consequences of management and procedures used in combating disease in order to determine the efficacy, effectiveness, safety, practicability, etc., of these interventions in individual cases or series. [NIH]

Trypsin: A serine endopeptidase that is formed from trypsinogen in the pancreas. It is converted into its active form by enteropeptidase in the small intestine. It catalyzes hydrolysis of the carboxyl group of either arginine or lysine. EC 3.4.21.4. [NIH]

Tryptophan: An essential amino acid that is necessary for normal growth in infants and for nitrogen balance in adults. It is a precursor serotonin and niacin. [NIH]

Tuberculosis: Any of the infectious diseases of man and other animals caused by species of Mycobacterium. [NIH]

Tuberous Sclerosis: A rare congenital disease in which the essential pathology is the appearance of multiple tumors in the cerebrum and in other organs, such as the heart or kidneys. [NIH]

Tubulin: A microtubule subunit protein found in large quantities in mammalian brain. It has also been isolated from sperm flagella, cilia, and other sources. Structurally, the protein is a dimer with a molecular weight of approximately 120,000 and a sedimentation coefficient of 5.8S. It binds to colchicine, vincristine, and vinblastine. [NIH]

Tumor marker: A substance sometimes found in an increased amount in the blood, other body fluids, or tissues and which may mean that a certain type of cancer is in the body. Examples of tumor markers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (prostate cancer). Also called biomarker. [NIH]

Tumor suppressor gene: Genes in the body that can suppress or block the development of cancer. [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]

Ultrafiltration: The separation of particles from a suspension by passage through a filter with very fine pores. In ultrafiltration the separation is accomplished by convective transport; in dialysis separation relies instead upon differential diffusion. Ultrafiltration occurs naturally and is a laboratory procedure. Artificial ultrafiltration of the blood is referred to as hemofiltration or hemodiafiltration (if combined with hemodialysis). [NIH]

Ultrasonography: The visualization of deep structures of the body by recording the reflections of echoes of pulses of ultrasonic waves directed into the tissues. Use of ultrasound for imaging or diagnostic purposes employs frequencies ranging from 1.6 to 10

megahertz. [NIH]

Unconscious: Experience which was once conscious, but was subsequently rejected, as the "personal unconscious". [NIH]

Uraemia: 1. An excess in the blood of urea, creatinine, and other nitrogenous end products of protein and amino acids metabolism; more correctly referred to as azotemia. 2. In current usage the entire constellation of signs and symptoms of chronic renal failure, including nausea, vomiting anorexia, a metallic taste in the mouth, a uraemic odour of the breath, pruritus, uraemic frost on the skin, neuromuscular disorders, pain and twitching in the muscles, hypertension, edema, mental confusion, and acid-base and electrolyte imbalances. [EU]

Uranium: A radioactive element of the actinide series of metals. It has an atomic symbol U, atomic number 92, and atomic weight 238.03. U-235 is used as the fissionable fuel in nuclear weapons and as fuel in nuclear power reactors. [NIH]

Urea: A compound (CO(NH2)2), formed in the liver from ammonia produced by the deamination of amino acids. It is the principal end product of protein catabolism and constitutes about one half of the total urinary solids. [NIH]

Uremia: The illness associated with the buildup of urea in the blood because the kidneys are not working effectively. Symptoms include nausea, vomiting, loss of appetite, weakness, and mental confusion. [NIH]

Ureter: One of a pair of thick-walled tubes that transports urine from the kidney pelvis to the bladder. [NIH]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

Uric: A kidney stone that may result from a diet high in animal protein. When the body breaks down this protein, uric acid levels rise and can form stones. [NIH]

Urinalysis: Examination of urine by chemical, physical, or microscopic means. Routine urinalysis usually includes performing chemical screening tests, determining specific gravity, observing any unusual color or odor, screening for bacteriuria, and examining the sediment microscopically. [NIH]

Urinary: Having to do with urine or the organs of the body that produce and get rid of urine. [NIH]

Urinary tract: The organs of the body that produce and discharge urine. These include the kidneys, ureters, bladder, and urethra. [NIH]

Urinary tract infection: An illness caused by harmful bacteria growing in the urinary tract. [NIH]

Urinate: To release urine from the bladder to the outside. [NIH]

Urine: Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Urogenital: Pertaining to the urinary and genital apparatus; genitourinary. [EU]

Urology: A surgical specialty concerned with the study, diagnosis, and treatment of diseases of the urinary tract in both sexes and the genital tract in the male. It includes the specialty of andrology which addresses both male genital diseases and male infertility. [NIH]

Vaccine: A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. [NIH]

Vacuoles: Any spaces or cavities within a cell. They may function in digestion, storage, secretion, or excretion. [NIH]

Valine: A branched-chain essential amino acid that has stimulant activity. It promotes muscle growth and tissue repair. It is a precursor in the penicillin biosynthetic pathway. [NIH]

Varices: Stretched veins such as those that form in the esophagus from cirrhosis. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

Vasculitis: Inflammation of a blood vessel. [NIH]

Vasodilation: Physiological dilation of the blood vessels without anatomic change. For dilation with anatomic change, dilatation, pathologic or aneurysm (or specific aneurysm) is used. [NIH]

Vasodilator: An agent that widens blood vessels. [NIH]

Vasopressins: Octapeptide antidiuretic hormones released by the neurohypophysis of all vertebrates (chemical composition varies with species). They control water metabolism and balance by regulating lung, gill, kidney, etc., and water loss, and also contract smooth muscle. They may also be neurotransmitters. Also included are synthetic vasopressin derivatives. Vasopressins are used pharmacologically as renal agents, vasoconstrictor agents, and hemostatics. [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]

Ventilation: 1. In respiratory physiology, the process of exchange of air between the lungs and the ambient air. Pulmonary ventilation (usually measured in litres per minute) refers to the total exchange, whereas alveolar ventilation refers to the effective ventilation of the alveoli, in which gas exchange with the blood takes place. 2. In psychiatry, verbalization of one's emotional problems. [EU]

Ventral: 1. Pertaining to the belly or to any venter. 2. Denoting a position more toward the belly surface than some other object of reference; same as anterior in human anatomy. [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]

Vertebrae: A bony unit of the segmented spinal column. [NIH]

Vertebral: Of or pertaining to a vertebra. [EU]

Vertebral Artery: The first branch of the subclavian artery with distribution to muscles of the neck, vertebrae, spinal cord, cerebellum and interior of the cerebrum. [NIH]

Vertebral Artery Dissection: Dissection of the wall of the vertebral artery, leading to the formation of an aneurysm that may occlude the vessel. Thrombus formation may occur and give rise to emboli. Cervical fractures or related neck injuries and craniocerebral trauma are commonly associated conditions, although this process may occur spontaneously. Ischemia, infarction, and hemorrhage in the vascular distribution of the affected vertebral artery may complicate this condition. [NIH]

Vesicoureteral: An abnormal condition in which urine backs up into the ureters, and occasionally into the kidneys, raising the risk of infection. [NIH]

Vesicular: 1. Composed of or relating to small, saclike bodies. 2. Pertaining to or made up of vesicles on the skin. [EU]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

Villous: Of a surface, covered with villi. [NIH]

Vinculin: A cytoskeletal protein associated with cell-cell and cell-matrix interactions. The amino acid sequence of human vinculin has been determined. The protein consists of 1066 amino acid residues and its gene has been assigned to chromosome 10. [NIH]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Viral vector: A type of virus used in cancer therapy. The virus is changed in the laboratory and cannot cause disease. Viral vectors produce tumor antigens (proteins found on a tumor cell) and can stimulate an antitumor immune response in the body. Viral vectors may also be used to carry genes that can change cancer cells back to normal cells. [NIH]

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]

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]

Vitamin A: A substance used in cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Vitreous Hemorrhage: Hemorrhage into the vitreous body. [NIH]

Vitro: Descriptive of an event or enzyme reaction under experimental investigation occurring outside a living organism. Parts of an organism or microorganism are used together with artificial substrates and/or conditions. [NIH]

Vivo: Outside of or removed from the body of a living organism. [NIH]

Weight Gain: Increase in body weight over existing weight. [NIH]

White blood cell: A type of cell in the immune system that helps the body fight infection and disease. White blood cells include lymphocytes, granulocytes, macrophages, and others. [NIH]

Withdrawal: 1. A pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality disorders. 2. (DSM III-R) A substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

Wound Healing: Restoration of integrity to traumatized tissue. [NIH]

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]

Xenograft: The cells of one species transplanted to another species. [NIH]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to

treat cancer. [NIH]

Yeasts: A general term for single-celled rounded fungi that reproduce by budding. Brewers' and bakers' yeasts are Saccharomyces cerevisiae; therapeutic dried yeast is dried yeast. [NIH]

Zalcitabine: A dideoxynucleoside compound in which the 3'-hydroxy group on the sugar moiety has been replaced by a hydrogen. This modification prevents the formation of phosphodiester linkages which are needed for the completion of nucleic acid chains. The compound is a potent inhibitor of HIV replication at low concentrations, acting as a chain-terminator of viral DNA by binding to reverse transcriptase. Its principal toxic side effect is axonal degeneration resulting in peripheral neuropathy. [NIH]

Zidovudine: A dideoxynucleoside compound in which the 3'-hydroxy group on the sugar moiety has been replaced by an azido group. This modification prevents the formation of phosphodiester linkages which are needed for the completion of nucleic acid chains. The compound is a potent inhibitor of HIV replication, acting as a chain-terminator of viral DNA during reverse transcription. It improves immunologic function, partially reverses the HIV-induced neurological dysfunction, and improves certain other clinical abnormalities associated with AIDS. Its principal toxic effect is dose-dependent suppression of bone marrow, resulting in anemia and leukopenia. [NIH]

Zymogen: Inactive form of an enzyme which can then be converted to the active form, usually by excision of a polypeptide, e. g. trypsinogen is the zymogen of trypsin. [NIH]

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